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SYNTHETIC STUDIES RELATED TO STERPURIC ACID

BY

© KEITH THOMAS HOGAN

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE

OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA

FALL 1986

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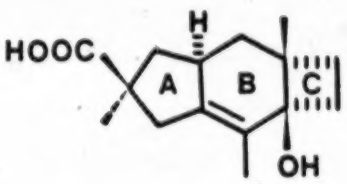
To my parents

ABSTRACT

This thesis describes the development of methodologies applicable to the synthesis of the BC ring system of the sesquiterpene sterpuric acid (1).



Sterpuric acid

(1)

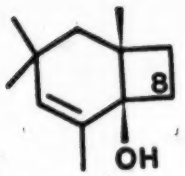
The carbon framework of the model compound 22 was constructed by a [2+2]intramolecular photocycloaddition of enone 24 to give photoadduct 25 with the required cis-ring junction stereochemistry. Enone 24 was prepared by treatment of alcohol 31 with vinyl chloroformate. The intramolecular photocycloadditions of three other cyclohexenones, 63, 64, and 65, were also investigated.

The six-membered ring of 22 was elaborated by treating ketone 25 with methyllithium followed by dehydration of the resultant tertiary alcohol to give alkene 108. The completion of the four-membered ring of 22 proved to be more difficult. Wittig methylenation of ketone 25 followed by basic hydrolysis led to diol 61. Monomesylation of diol 61 followed by attempted

displacement with a variety of nucleophiles led initially to ketone 89 rather than the desired displacement product. The stereospecificity of this rearrangement is discussed.

The successful deoxygenation at C-8 involved Swern oxidation of diol 61 to ketone 98 followed by acetylation of the tertiary alcohol of 98, tosylhydrazone formation, and reduction of the hydrazone to give compound 26.

Another route to 22 involved the formation of the vinylthio analogue 127. The successful route involves acylating alcohol 31 with S-(β -chloroethyl) chlorothiolformate to give the chloro derivative 143. Chloride 143 was converted to iodide 145 and then to selenide 148. Oxidation of selenide 148 led to thioalkene 127. A [2+2]intramolecular photocycloaddition of thioalkene 127 gave photoadduct 128 with the required cis-ring junction stereochemistry. The conversion of photoadduct 128 to compound 22 is discussed.



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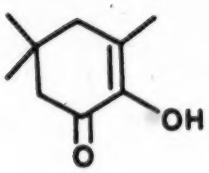

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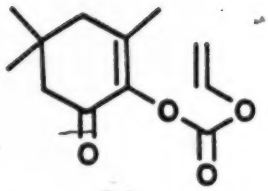

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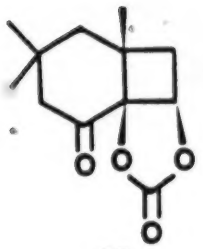

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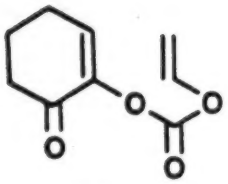

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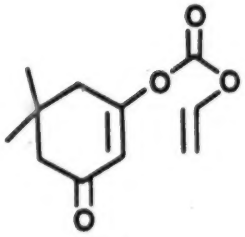

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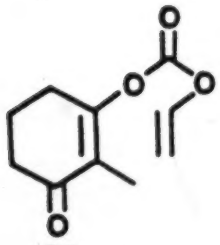

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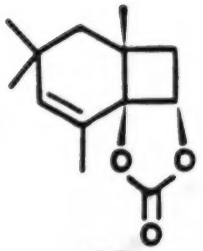

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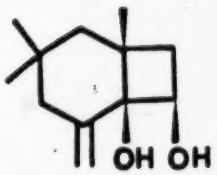

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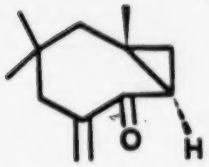

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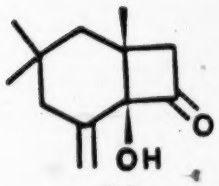

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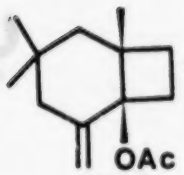

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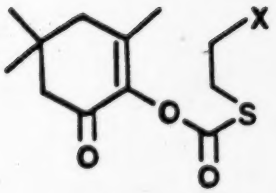
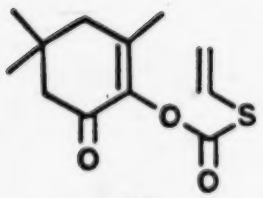


143 X=Cl

145 X=I

148 X=ArSe



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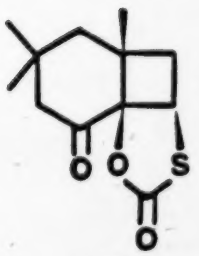

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ABBREVIATIONS

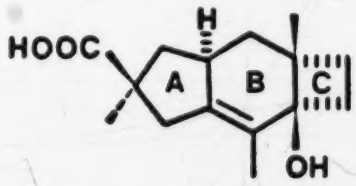
nmr	nuclear magnetic resonance
ir	infrared
nOe	nuclear Overhauser enhancement
gc	gas chromatography
tlc	thin layer chromatography
W	watt
M	molar
ptlc	preparative thin layer chromatography
GASPE	gated spin echo experiments
r.t.	room temperature
eq.	equivalent
Ac_2O	acetic anhydride
Et_3N	triethylamine
4-DMAP	4-N,N-dimethylaminopyridine
$Ar_3P{=}CH_2$	methylenetriphenylphosphorane
DME	1,2-dimethoxyethane
ArH	benzene
DMSO	dimethylsulfoxide
NaH	sodium hydride
MsCl	methanesulfonyl chloride
ArSeSeAr	diphenyldiselenide
HMPA	hexamethylphosphoric triamide
HMDS	hexamethyldisilizane

TMSCl	trimethylsilyl chloride
Ar_3P	triphenylphosphine
$\underline{n}$-Bu_4NOAc	tetra-$\underline{n}$-butylammonium acetate
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
KO^tBu	potassium $\underline{tert}$-butoxide
h	hours
min	minutes
dec	decomposes

I. INTRODUCTION

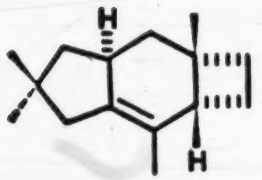
Sterpuric acid (1) is a novel sesquiterpenoid isolated by Ayer and co-workers[1] in 1981. It is a metabolite produced by Stereum purpureum (Pers. ex Fr.) Pouzar, the fungus responsible for the so-called silver leaf disease of mountain ash, plum, apple, and other fruit trees. S. purpureum produces four other natural products, 2 - 5, which have the same tricyclic skeleton as compound 1. Biosynthetic studies have confirmed the sesquiterpenoid nature of the compound.[1b]

The structure of sterpuric acid was deduced from a combination of chemical transformations and spectroscopic analyses and was unequivocally confirmed by X-ray crystallographic studies. The absolute configuration has not been determined. The B and C rings of sterpuric acid comprise a bicyclo[4.2.0]octane system. During the last

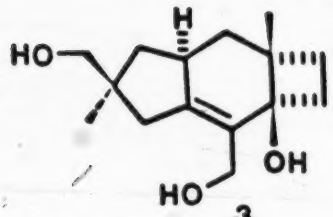


Sterpuric acid

(1)


H
H

2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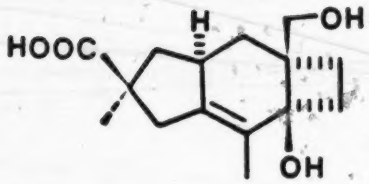
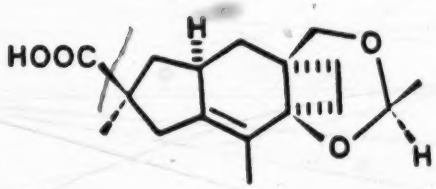
OH
HO

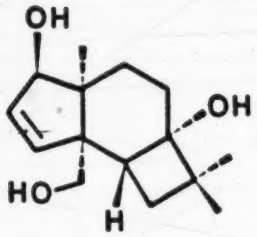
3


HOOC
H
OH
OH

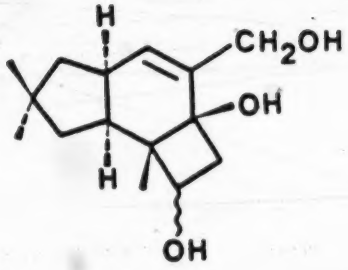
4


HOOC
H
O
O
H

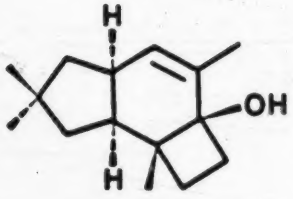
5


OH
OH
HO
H

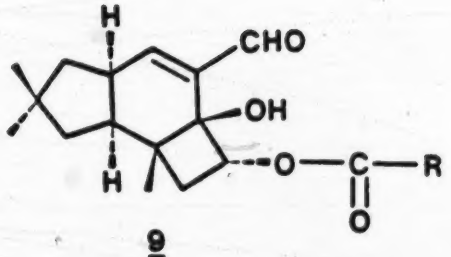
6


H
CH2OH
OH
H
OH

7


H
OH
H

8

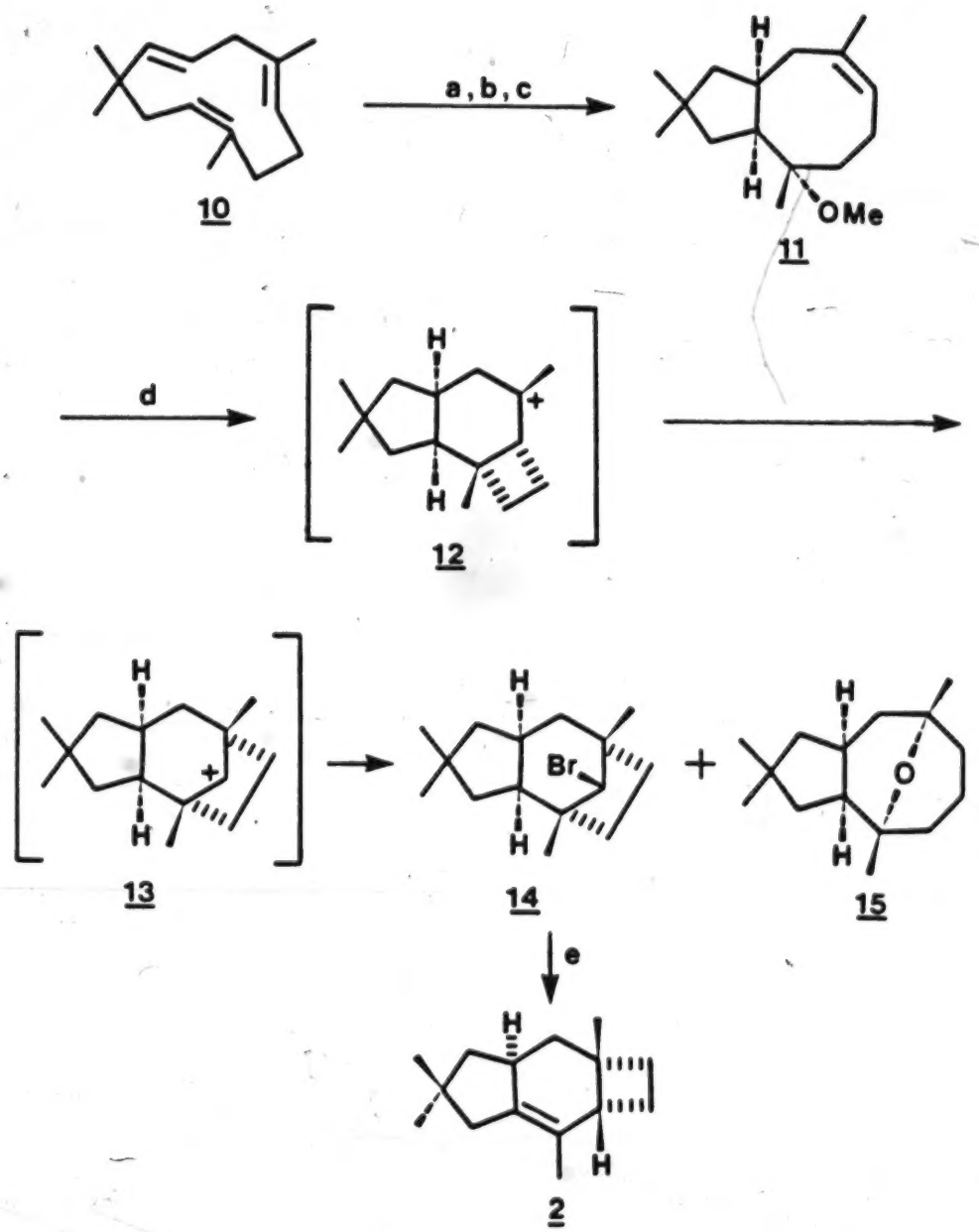

H
CHO
OH
H
O
C
R
O

9

10 years over fifteen such compounds have been isolated from natural sources. Some pertinent members of this group include punctatin A (6)[2], neoilludol (7)[3], Δ^7-protoilluden-6-ol (8)[4], and melleolide (9)[5].

Since sterpuric acid represents a new class of sesquiterpenoids few synthetic efforts toward this class of compounds have appeared in the literature. Two syntheses of this class of compounds have recently been completed but the results have not, as yet, been published. B.M. Trost and co-workers[6] have synthesized sterpuric acid (1) while R.D. Little and co-workers[7] have prepared sterpurene (2). Matsumoto and co-workers[8] have successfully synthesized sterpurene (2) by a biomimetic approach (Scheme 1). They were able to convert humulene (10) to 2 via the protoilludyl cation 12, mimicing the reported biosynthetic pathway of this class of compounds. The methyl ether 11, prepared from 10, was treated with boron tribromide to give bromide 14 (21%) and ether 15 (21%). The course of the reaction to form bromide 14 may be interpreted in the following way:[9] the methyl ether 11 furnished first the protoilludyl cation 12 which rearranged to cation 13 to give concertedly the bromide 14. Treatment of bromide 14 with silver acetate furnished sterpurene (2).

Scheme 1. Formation of sterpurene (2) from humulene (10)[8]



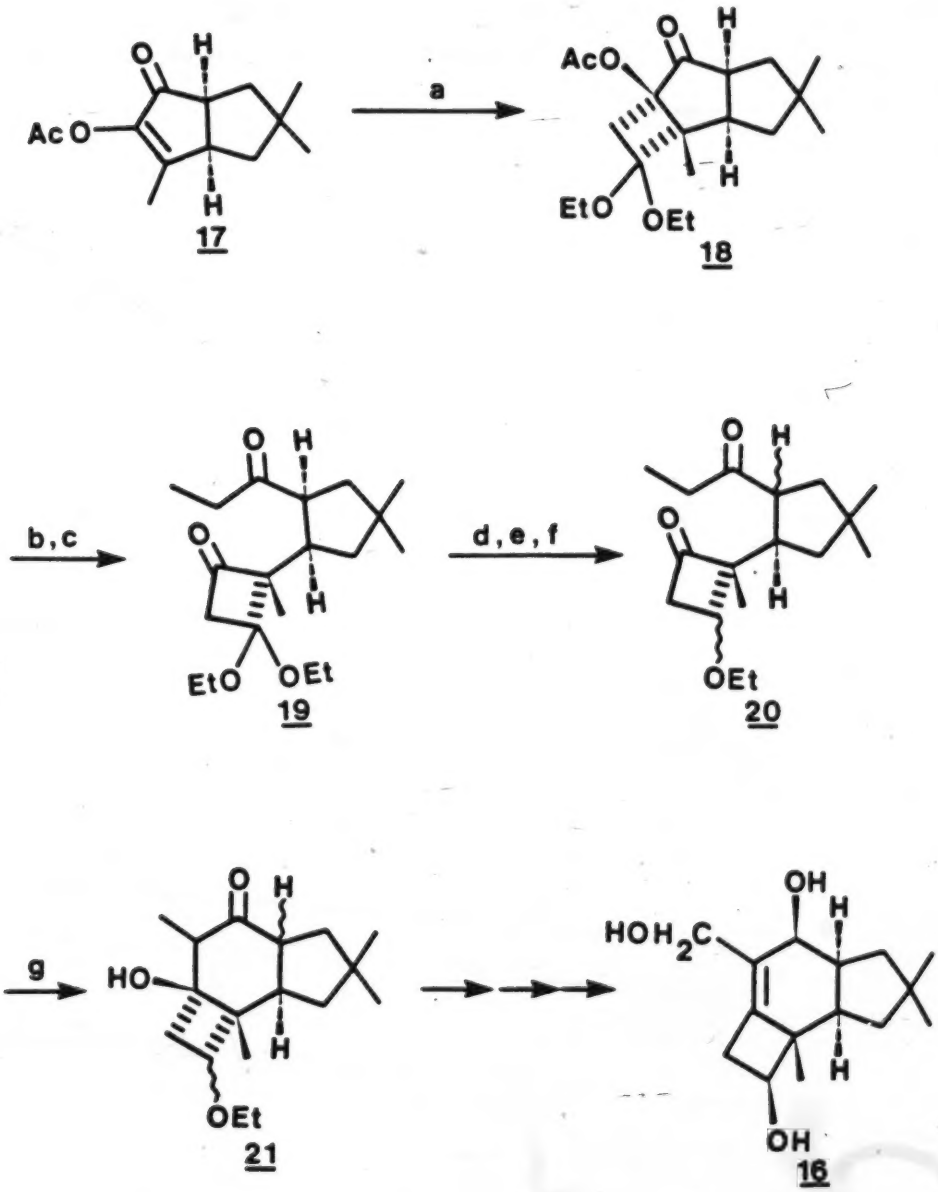
10 11 12 13 14 15 2

a. $Hg(NO_3)_2$ b. Li-$EtNH_2$ c. NaH, MeI d. BBr_3
e. AgOAc, AcOH, 90°C

The bicyclo[4.2.0]octane synthesis most relevant to the synthesis of 1 is that of Matsumoto who prepared illudol (16)[10] (Scheme 2). A key aspect of the synthesis was the formation of the cyclobutane ring by a [2+2] intermolecular photocycloaddition of cyclopentenone 17 with 1,1-diethoxyethylene to form the tricyclic compound 18. The approach takes advantage of the transformation of a bicyclo[3.2.0]heptane system, the B and C rings of 18, to a bicyclo[4.2.0]octane system, the B and C rings of 21. Compound 18 was treated with ethylmagnesium bromide and the resulting diol was oxidized to the diketone 19. A series of functional group transformations converted diketone 19 into diketone 20. Aldol condensation of this compound resulted in the formation of alcohol 21. The stereochemistry at the cyclobutane ring junction of 21 was not defined although from steric considerations it is assumed to be cis. This compound was subsequently converted into illudol (16) in a number of steps.

Since sterpuric acid (1) possesses a novel skeleton and may have interesting biological activity, we initiated a research project aimed at developing an efficient synthesis of the BC ring system of 1. We chose compound 22 as our bicyclo[4.2.0]octane model since it closely resembles the BC ring system of 1 and the cyclohexyl

Scheme 2. Matsumoto's synthesis of illudol (16)[10]



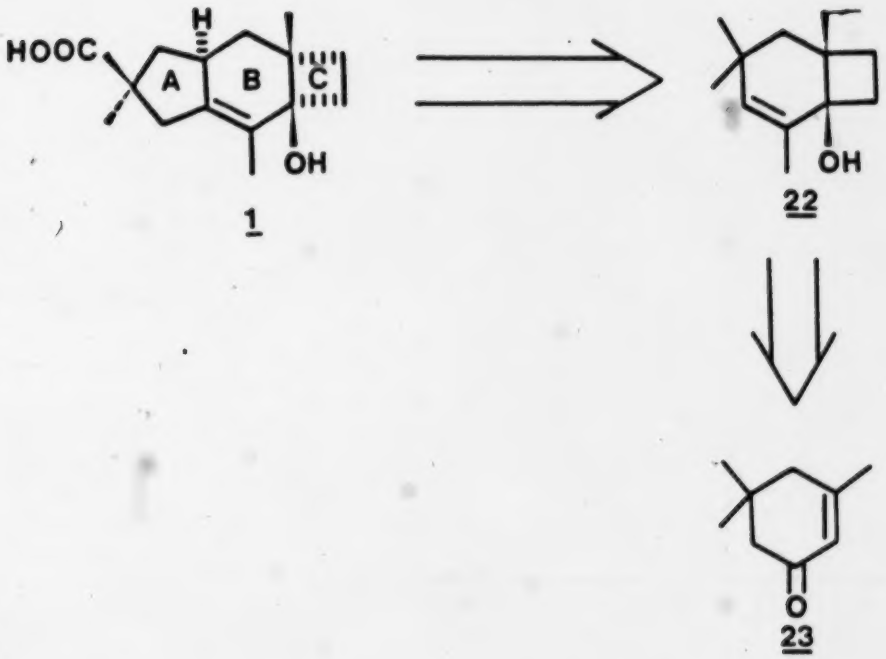
a. hv, CH_2=C(OEt)$_2$, 50% b. EtMgBr c. $NaIO_4$ d. basic alumina e. $NaBH_4$ f. Jones oxid. g. 1 N KOH

portion could be derived from readily available isophorone (23) (Scheme 3).

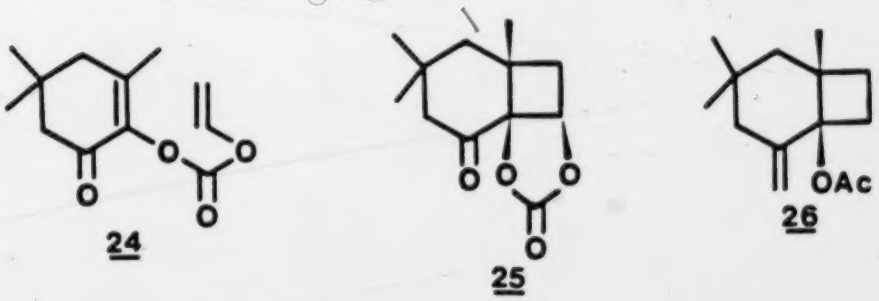
A highly stereo- and regioselective synthesis of a precursor of 22 was achieved in our laboratory. The synthesis utilizes a novel [2+2]intramolecular photocycloaddition reaction of 24 to form a key intermediate 25. Subsequent modification of this compound to 26 furnished the desired cis-bicyclo[4.2.0]octane system.

Three other methods for the synthesis of 22 from 23 were also examined. In the first route a [2+2] intermolecular photocycloaddition was explored as a means of controlling the stereochemistry at C-1 and C-6 of 22 and of incorporating the necessary functionality for further elaboration of the cyclohexyl ring. In the second route the nucleophilic addition of an acetate anion via a cine substitution reaction to a bicyclo[4.2.0]octanone precursor was envisaged as a plausible solution towards introduction of the oxygen substituent at C-1 of 22. The third route involves the formation of a vinylthio analog of 24 which could provide 22.

Scheme 3. Retrosynthesis of the BC ring system of Sterpuric Acid (1)



1 22 23



24 25 26

The results of these investigations will be discussed in this thesis. To facilitate the presentation, the discussion is broken down into the following six topics:

1. [2+2]intermolecular photocycloadditions
2. [2+2]thermal cycloadditions and cine substitution reaction
3. [2+2]intramolecular photocycloadditions of 2- and 3-[(2-oxabut-3-enoyl)oxy]cyclohex-2-enones
4. Transformation of the model bicyclo[4.2.0]compound to a BC ring intermediate
5. Examination of the pinacol rearrangement of bicyclo-[4.2.0]octane-1,8-diols
6. Formation and transformation of a 2-[(2-thiabut-3-enoyl)oxy]cyclohex-2-enone.

II. RESULTS AND DISCUSSION

1. [2+2]Intermolecular Photocycloadditions

A strategy for the synthesis of 22 from 23 must involve the formation of a four-membered ring with a ring junction oxygen substituent. Compound 23 is suitably functionalized such that it may be modified to give the desired functionality in the six-membered ring of compound 22. We felt that construction of the bicyclic ring system with the desired ring junction substituents in the required cis orientation would be a challenging aspect of the synthesis of sterpuric acid (1).

Although four-membered rings can be formed by ionic pathways[11b], we concentrated our efforts on the various known [2+2]cycloaddition reactions. A review of the literature indicated that these reactions are the methods of choice for the formation of four-membered ring compounds with high stereo- and regiochemical control.

Yamada[12] has described the [2+2]intermolecular photocycloaddition* of enone 23 with ethylene to give bicycloketone 27. We felt that compound 28 may undergo a similar photocycloaddition reaction with ethylene to give

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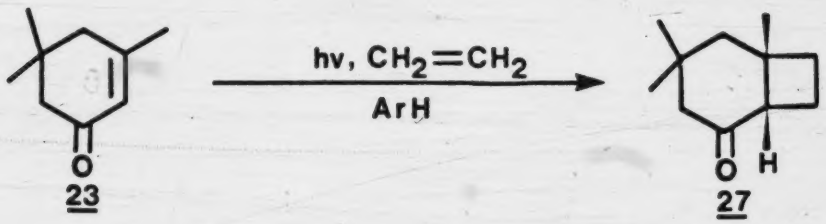
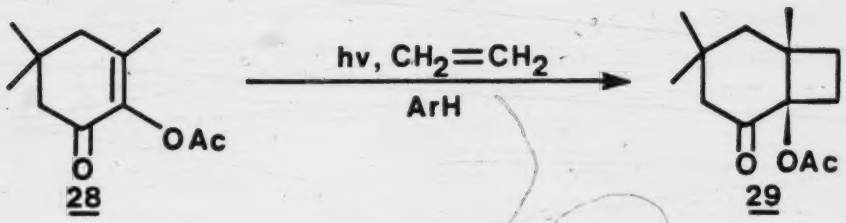
*For a review of [2+2]intermolecular photocycloadditions see reference 11.

bicyclic ketoacetate 29. Compound 29 could then be transformed to the desired compound 22. The acetoxyl substituent at C-2 in 28 would provide the ring junction oxygen substituent of 22.

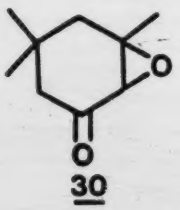


23 27



28 29

Compound 28 was prepared in three steps from isophorone (23). Treatment of 23 with basic hydrogen peroxide gave epoxyketone 30 which was converted into the known ketoalcohol 31 by an acid-catalyzed rearrangement.[13]



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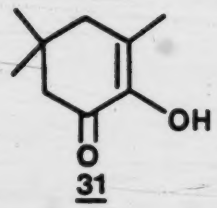

31

Acetylation (pyridine, Ac_2O) of 31 gave enone 28 in 88% yield.

Ethylene was bubbled into a degassed benzene solution of enone 28 contained in a quartz immersion well photochemical reactor. Irradiation of the solution with a 450-W medium pressure mercury lamp did not lead to reaction. After 112 hours enone 28 was recovered. Modification of the reaction conditions by using other solvents (Skellysolve B, acetone), filters (Corex, Pyrex, Vycor) or adding sensitizers (acetophenone) did not induce the desired cycloaddition.

Photolysis of enone 28 with other alkene equivalents such as acetylene, vinyl acetate, 1,2-dichloroethylene, or the reactive 1,1-diethoxyethylene[14] under a variety of conditions also failed to give a [2+2]photoadduct. It is surprising that 1,1-diethoxyethylene does not undergo photocycloaddition with ketoacetate 28 since it reacts readily with the corresponding cyclopentenone 17 (vide supra).[10] Presumably the C-2 acetoxyl group of 28 reduces the reactivity of the enone towards photoaddition. It is known that 2-alkylsubstituted cyclohexenones unlike 2-alkylsubstituted cyclopentenones do not undergo intermolecular photocycloaddition reactions with alkenes[15] and alkynes[16] very efficiently.

2. [2+2]Thermal Cycloadditions and Cine Substitution Reaction

We also investigated the introduction of a ring junction oxygen substituent to a preformed bicyclo[4.2.0]-octanone ring system. This approach had been demonstrated previously by Harding[17] with the dichlorobicyclo[4.2.0]-octanone 32 (Scheme 4). He showed that acetate anion displaces a chlorine of a dichloroketone such as 32 in a regiospecific manner to give chloroacetate 33 in what is referred to as a cine substitution reaction.*

The reaction is thought to proceed through the intermediate enol 34. The acetate anion attacks the convex face of 34 producing a cis-bicyclooctanone 33. We decided to explore this strategy for the preparation of the BC ring system of 1 and chose dichloroketone 35 for our model studies (Scheme 5). Although compound 35 has a methyl group at one ring junction we felt that the acetate anion should still attack from the convex side producing the desired cis-ring junction.

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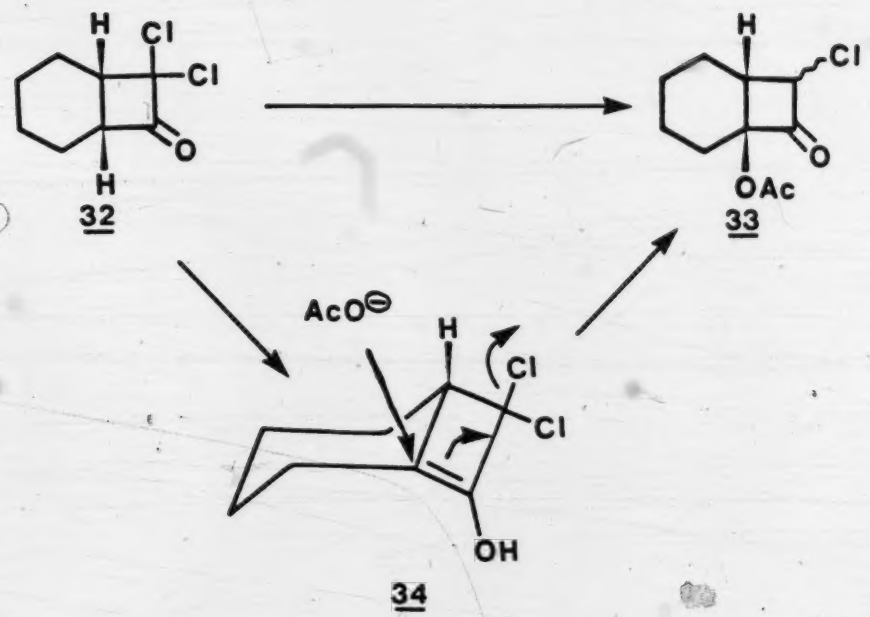
*Cine substitution refers to attack of the nucleophile at a site removed from the leaving group.

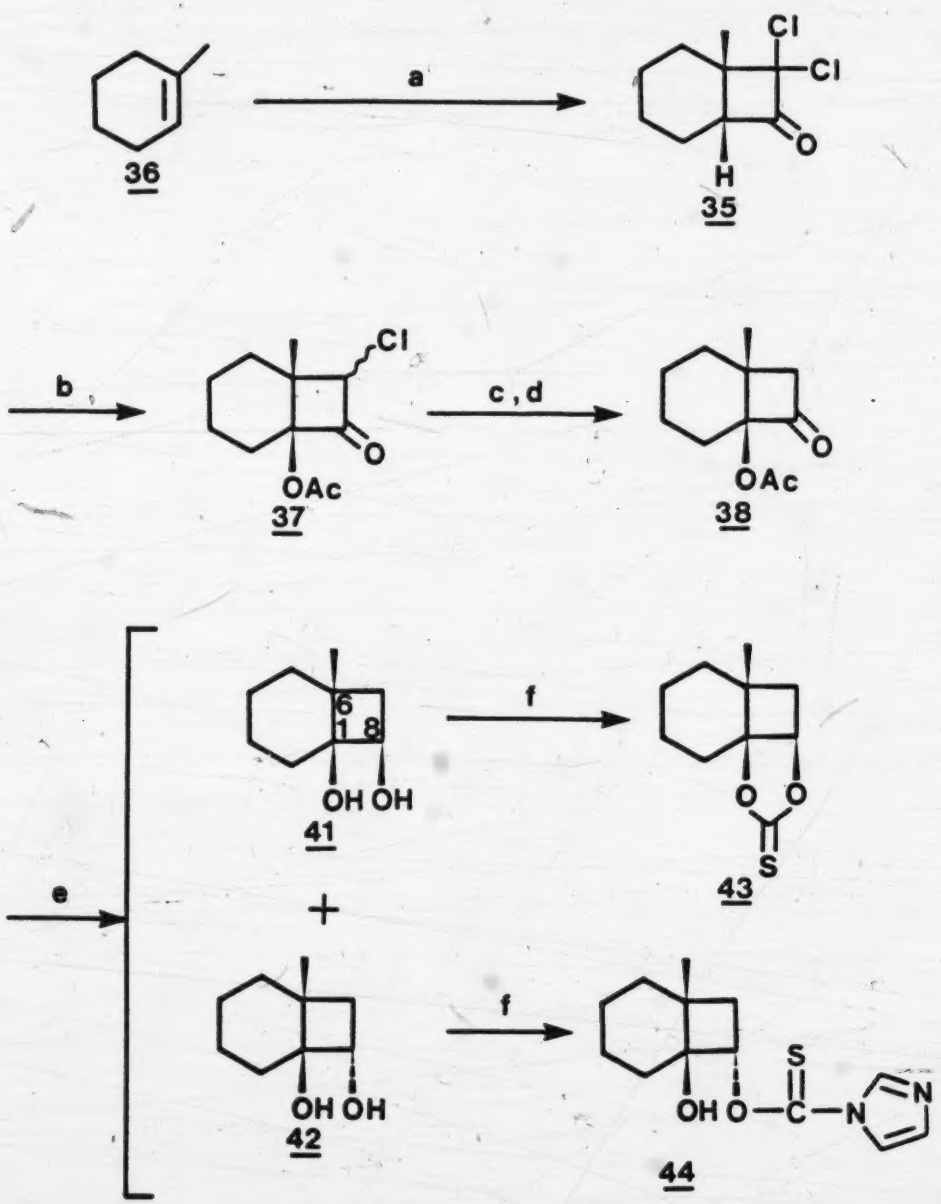
Scheme 4. Introduction of a ring junction oxygen functionality to 32



Dichloroketone 35 was prepared by a [2+2]thermal cycloaddition* reaction between 1-methylcyclohexene 36 and dichloroketene according to the method of Krepski.[18] Only one regioisomer is formed, that in which the most nucleophilic carbon atom of the olefin is bonded to the sp hybridized carbon atom of the ketene molecule. The reaction of dichloroketene with olefins is known to give a stereospecific cis cycloaddition product and thus a cis stereochemistry can be assigned to compound 35.

*For a review of [2+2]thermal cycloadditions see reference 19.

Scheme 5. Synthesis of cis-fused 38 and derivatives

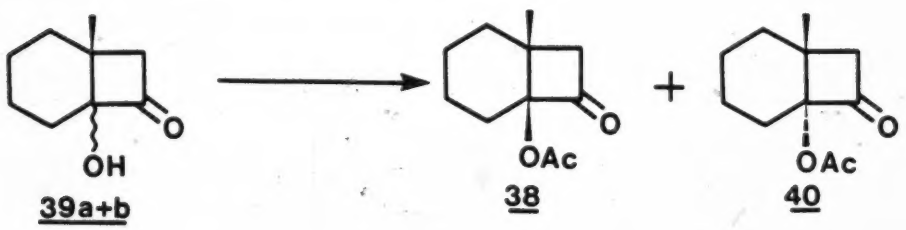


a) Zn(Cu) couple, Cl_3CCOCl, $POCl_3$, Et_2O, reflux b) Et_3NHOAc c) $CrCl_2$, H_2SO_4 d) Et_3N, Ac_2O, 4-DMAP, CH_2Cl_2 e) $LiAlH_4$, Et_2O f) 1,1'-thiocarbonyldiimidazole, $ClCH_2CH_2Cl$, reflux

Dichloroketone 35 was treated with one equivalent of triethylammonium acetate to give chloroacetate 37 which was used directly in the next step. Dechlorination of 37 was effected by treatment with an excess of chromous chloride at room temperature for 5 hours. Since the reduction was carried out in the presence of acid, partial hydrolysis of the acetoxyl group occurred (^{1}H nmr, ir, tlc). The crude reaction mixture was acetylated (Et_3N, Ac_2O, 4-DMAP) to give ketoacetate 38 in 82% yield from 35. The mass spectrum of 38 displays a molecular ion at m/z 196.1102 corresponding to the molecular formula $C_{11}H_{16}O_2$. ^{1}H and ^{13}C nmr spectra of 38 indicate that the adduct is a single stereoisomer. In particular the ^{13}C nmr spectrum of 38 shows signals at δ203.0 (cyclobutyl ketone), δ 169.4 (acetoxyl carbonyl) and δ 90.7 (quaternary carbon bonded to an oxygen substituent). In the ^{1}H nmr spectrum of 38 the methylene protons α to the ketone appear as an AB pattern (δ 3.08, δ 2.52) with J_{AB}=17 Hz.

Interestingly, if the chromous chloride reduction of chloroketone 37 is allowed to proceed for 64 hours, a mixture of 2 stereoisomeric ketoalcohols 39a+b is obtained as evidenced by ^{1}H nmr. Acetylation (*vide supra*) of this mixture gave a 49% overall yield (from 35) of two stereoisomeric ketoacetates 38 and 40 in a ratio of 4:1

(^{1}H nmr). Small amounts of pure 38 and 40 were separated for analysis by ptlc. Spectral analysis of the separated isomers reveals that the major product of the reduction is ketoacetate 38. The minor product 40 has similar spectral properties and the ^{1}H and ^{13}C nmr of 40 indicate that it is epimeric to 38. In particular the ^{1}H nmr spectrum of the minor isomer 40 shows an AB pattern (δ 2.42, δ 2.27) for the methylene protons α to the ketone with J_{AB}=11 Hz.



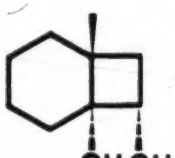
We were unable to assign the stereochemistry of the ring junction in 38. However, conversion of 38 to a derivative allowed us to make the stereochemical assignment. Reduction of 38 with lithium aluminum hydride gave a 1:1 mixture of diols 41 and 42 which were easily separated by flash chromatography. Since ketoacetate 38 is a single isomer the diols are presumed to be epimeric at C-8. This was supported by ir studies. Dilution studies reveal that the hydrogen bonded O-H stretching absorption disappears upon dilution[20] of diol 42. Such is not the case with diol 41. This indicates that the two

hydroxyl groups in diol 41 are cis whereas the hydroxyl groups in diol 42 are trans. Derivatives of the diols lend further support to this assignment. Cis-diol 41 reacted with 1,1'-thiocarbonyldiimidazole[21] to give cyclic thiocarbonate 43 while trans-diol 42 reacted to give alcohol 44.

With cis-diol 41 in hand the stereochemistry of the ring junction could be determined by ^1H nmr solvent studies utilizing deuterochloroform ($CDCl_3$) and pyridine-d_5.[22] It is known that the ^1H chemical shift of a methyl group oriented gauche with respect to a hydroxyl group will shift as much as 0.4 ppm in the different solvents. If the methyl group is anti with respect to the hydroxyl group no significant change in chemical shift is observed. In the case of diol 41 the methyl group at C-6 shows a large "pyridine shift" of -0.25 (δ $CDCl_3$ — δ pyridine-d_5) indicative of a cis relationship between the two hydroxyl groups at C-1 and C-8 and the methyl group at C-6. If the cis-diol possessed structure 45 it would not show a pyridine shift since both hydroxyl groups are trans to the methyl group. Thus ketoacetate 38 must have a cis-ring junction and its isomer, 40, must have a trans-ring junction.

Interestingly the trans-isomer 40 is found only when cis-ketoacetate 38 is completely hydrolysed to the

ketoalcohol. Presumably the acid present in the chromous chloride reduction of chloroketone 37 isomerizes the initially formed cis-ketoalcohol 39a to the trans-ketoalcohol 39b. This may occur via the intermediate radical 46.



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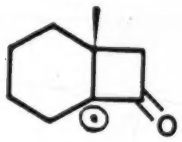
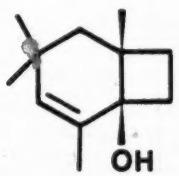


46

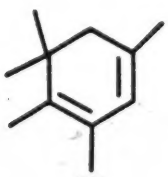
Since the cine substitution reaction does indeed form a cis-bicyclo[4.2.0]octanone with a ring junction methyl and oxygen substituent in a regiospecific and stereoselective manner, this method potentially could be useful in the synthesis of bicyclo[4.2.0]octanes such as 22.



22

In considering this synthetic strategy two points require further attention. Firstly, at some point in the

synthesis, the cyclobutane ring carbonyl that is formed must be reduced to a methylene group. Secondly, the cyclohexyl ring must be appropriately functionalized to allow the introduction of the endocyclic double bond and the methyl group at C-2. This functionality could be incorporated in the cyclohexene ring before dichloroketene addition. Initially we considered diene 47 as a possible starting material but there were sufficient literature precedents[23] to indicate that dichloroketene would add to 47 to give the wrong regioisomer; i.e., the regioisomer in which the carbon bearing the methyl group is bonded to the sp hybridized carbon of the ketene molecule. This



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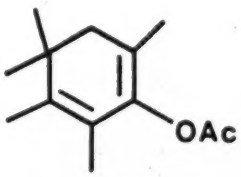

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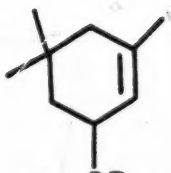
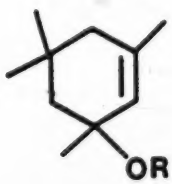


49 R=Me
51 R=H



50 R=Me
52 R=H

regioisomer could not undergo the desired cine substitution reaction to give a ring junction oxygen substituent. A starting material such as diene 48 in which the oxygen substituent is present could be used to react with dichloroketene but there are few literature precedents[24] on the reaction of dichloroketene with tetrasubstituted olefins.

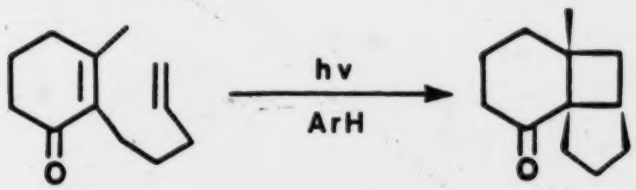
Two other potential starting materials, compounds 49 and 50, which might add dichloroketene to form the desired regioisomers were synthesized from isophorone. Isophorone was reduced with sodium borohydride to give alcohol 51 which was methylated with sodium hydride and methyl iodide to give methyl ether 49 in 71% overall yield. Isophorone was treated with methyllithium to give tertiary alcohol 52. This was treated with potassium hydride and methyl iodide to give methyl ether 50 in 68% overall yield.

Each of these compounds, 49 and 50, was separately treated with dichloroketene generated by the method of Krepski.[18a] In each case the desired bicyclooctane adducts could not be isolated in greater than 5% yield. Invariably the major products of the reactions were the cyclohexadienes resulting from the loss of the methoxyl groups. Although there are some literature precedents[25] for the reaction of functionalized 1-methylcyclohexenes

with dichloroketene we did not pursue this approach any further.

3. [2+2]Intramolecular Photocycloadditions of 2- and 3-[(2-Oxabut-3-enoyl)oxy]cyclohex-2-enones

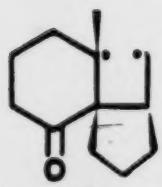
The [2+2]intramolecular photochemical cycloaddition* of an α, β-unsaturated ketone and an olefinic double bond was investigated for the formation of 22. We were encouraged by a recent report[26] that tricyclic compound 54 could be formed by a [2+2]intramolecular photocycloaddition of enone 53. This is in contrast to the usually inefficient intermolecular photoaddition of 2-alkylcyclohexenones[15, 16] (vide supra). Both the inter- and the intramolecular photocycloaddition reaction between an enone and an alkene proceed by the same mechanism. Excitation of the enone gives an excited singlet state



53 54

*For a review of [2+2]intramolecular photochemical cycloadditions see reference 27.

which undergoes intersystem crossing to the excited enone in its lowest triplet state. The excited enone adds to the alkene to give an intermediate biradical and eventually a cyclobutane. In contrast to the intermolecular version the intramolecular photocycloaddition, in which the olefinic double bond is connected to the enone by a chain of two to four atoms, usually occurs stereo- and regioselectively. The regioselectivity may be explained by the empirical rule of five[27a] which states that the favored ring system will be that derived from a biradical possessing a five-membered ring. This explains the formation of 54 from 53 since the formation of intermediate biradical 55 should be favored over intermediates 56a and 56b. Exceptions to the rule of five have been reported.[27a]



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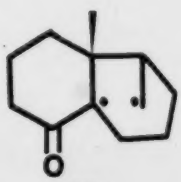
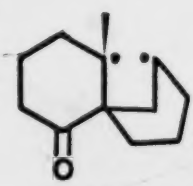


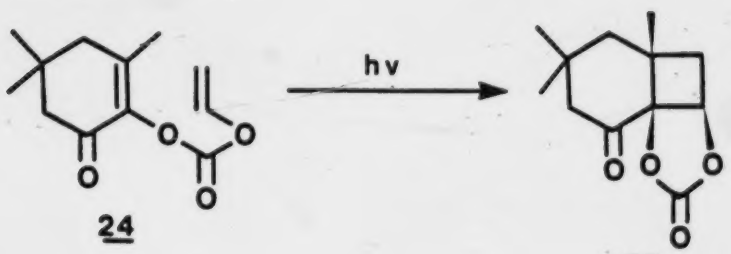
56a



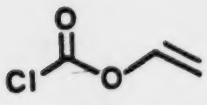
56b

We chose enone 24 as our photochemical substrate since photocycloaddition of 24 in a manner similar to 53 should form 25. Hydrolysis of the carbonate group of 25 would generate the desired cis-fused ring junction

containing the methyl and hydroxyl groups. Subsequent synthetic transformations should then lead to the target compound 22.



24 25



57

Enone 24 was readily formed in nearly quantitative yield by reaction of alcohol 31 with vinyl chloroformate (57). A degassed solution of 24 in acetone was irradiated through a Pyrex filter (1.5 mm, λ >283 mm) using a medium pressure 450-W mercury lamp in a quartz immersion well. This led to the formation of tricyclic compound 25 in 81% yield (based on starting material consumed). The reaction was monitored by gc and/or tlc and was stopped before all

the enone 24 had reacted.* Several reaction conditions including solvent, reaction time, and filter were varied in an attempt to improve the yield of 25. When solvents such as MeOH, Skellysolve B, CH_2Cl_2, THF, ArH, and CH_3CN were used significantly lower yields of photoadduct 25 were obtained. Best yields of 25 were obtained with acetone as solvent, presumably because acetone may also act as a sensitizer in the cycloaddition reaction.[28] The use of other sensitizers such as acetophenone and benzophenone in benzene did not improve the yield of 25.

Compound 25 is photoreactive under the reaction conditions. When long reaction times were employed a complex mixture of products was obtained. The best yields (>65%) of 25 are obtained when the cycloaddition reaction is stopped before 80% of enone 24 has been consumed (Table 1). Use of Pyrex filters (4.5 mm thick) or other filters such as soft glass ($\lambda > 293$ nm) or Uranium ($\lambda > 333$ nm)** did not increase the yield of 25. It has been reported that a tuneable laser dramatically improves the yields of

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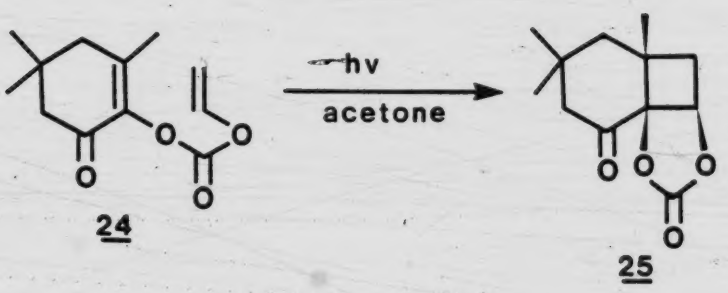
*If the reaction is allowed to go to completion yields of 40-45% are consistently obtained. The concentration of enone 24 was 0.004-0.06 M.

**When the Uranium glass filter was used, the photocycloaddition proceeded too slowly to be synthetically useful.

Table 1: Conversion of 24 to 25



24 25

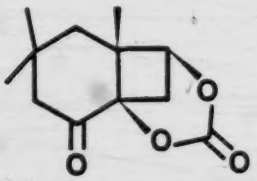
24 #g	Acetone (mL)	Time h*	Yield 25**	% of 24 consumed
4.50	500	34	81%	53%
2.26	500	24	66%	76%
0.21	200	4.5	57%	90%
0.22	200	5	44%	100%

*The time for completion of reaction was dependent on the concentration of 24.

**Based on starting material consumed

photoadducts in similar reactions[29] but this photosource was not available to us.

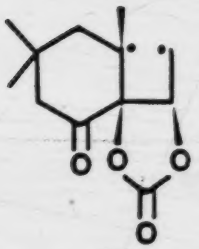
The structure of 25 was deduced from spectroscopic evidence and chemical studies. The ir spectrum of 25 shows absorption bands at 1810 cm^{-1} and 1725 cm^{-1} indicative of a five-membered ring carbonate and a six-membered ring ketone respectively. The ^{13}C nmr spectrum of 25 suggested the presence of the four-membered ring as evidenced by signals at δ87.6 (quaternary C-O) and δ 77.6 (secondary C-O). The ^{1}H nmr spectrum of 25 shows a methine signal at δ 5.02 (dd, J=5, 6 Hz) coupled to an adjacent methylene group, providing further evidence for the presence of the cyclobutane ring.



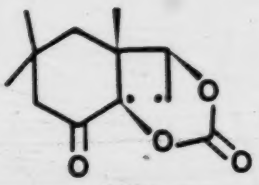
58

The regioisomer 58 may be ruled out since the ir of the product lacks the characteristic six-membered ring carbonate absorption at 1775 cm^{-1}.[30] Compound 58 is also

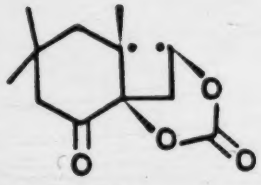
disfavored because its formation violates the rule of five since formation of the five-membered ring biradical 59 should be favored over the formation of the six-membered biradicals 60a and 60b.



59

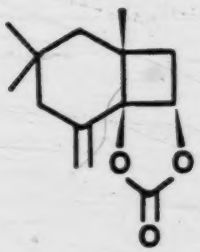


60a

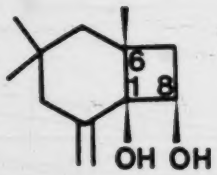


60b

The relative stereochemistry of the cyclobutane substituents in 25 was determined by converting 25 to diol 61. This was accomplished by Wittig methylenation ($Ar_3P{=}CH_2$) of ketone 25 to give 62 followed by basic hydrolysis (K_2CO_3, aqueous MeOH) of 62 to afford diol 61 in 89% overall yield from 25.



62



61

Dilution studies using ir spectroscopy clearly show that the hydrogen bonding absorption at 3520 cm^{-1} in the ir spectrum of 61 does not disappear in very dilute solution. This result suggests that the two hydroxyl groups have a cis relationship in compound 61.[20] When the ^1H nmr spectrum of 61, recorded in deuterochloroform, is compared with that recorded in pyridine-d_5, a pyridine shift (δ $CDCl_3$ — δ pyridine-d_5) of -0.16 is observed for the signal assigned to the C-6 methyl.[22] Such a shift indicates that the C-6 methyl is cis to the hydroxyl groups at C-1 and C-8. Thus compounds 61 and 25 have the relative stereochemistry indicated. These results were confirmed by an X-ray crystallographic study* of 25.

Three other vinyl carbonates, 63, 64, and 65, were synthesized to test the generality of the photocyclization. Compounds 63 - 65 were prepared in nearly quantitative yields by treating the corresponding enols with vinyl chloroformate (57) in the presence of pyridine.

Irradiation of a degassed solution of 63 in acetone through a Pyrex filter (1.5 mm) using a 250-W medium pressure mercury lamp resulted in the formation of

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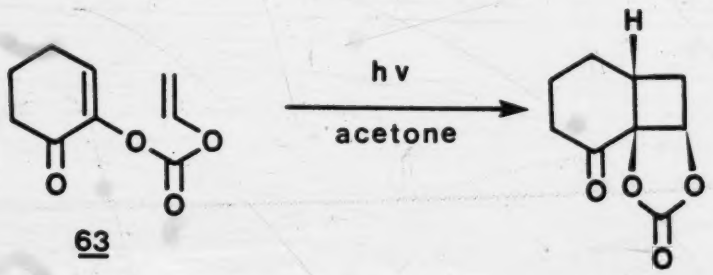
*L.T.J. Delbaere, private communication.

tricyclic compound 66 in 65% yield* (based on starting material consumed). The five-membered ring carbonate was formed as evidenced by an absorption at 1801 cm^{-1} in the ir spectrum of 66 and by a methine signal at δ 5.00 (dd, J=4.5, 6.5 Hz) in its ^1H nmr spectrum.



63 66

The 3-substituted cyclohex-2-enones, compounds 64 and 65, did not undergo the intramolecular photocycloaddition reactions as efficiently as the 2-substituted derivatives 24 and 63. When enone 64 was irradiated (450-W medium pressure mercury lamp, Pyrex filter, quartz immersion well) and the reaction was interrupted when ca. 70% of the starting material had been consumed, two major products, 67 and 68, were obtained in 20% and 10% yields respectively (Scheme 6). Ir analysis of each product indicated the presence of hydroxyl groups, thus the corresponding monoacetate derivatives, 69 and 70, were

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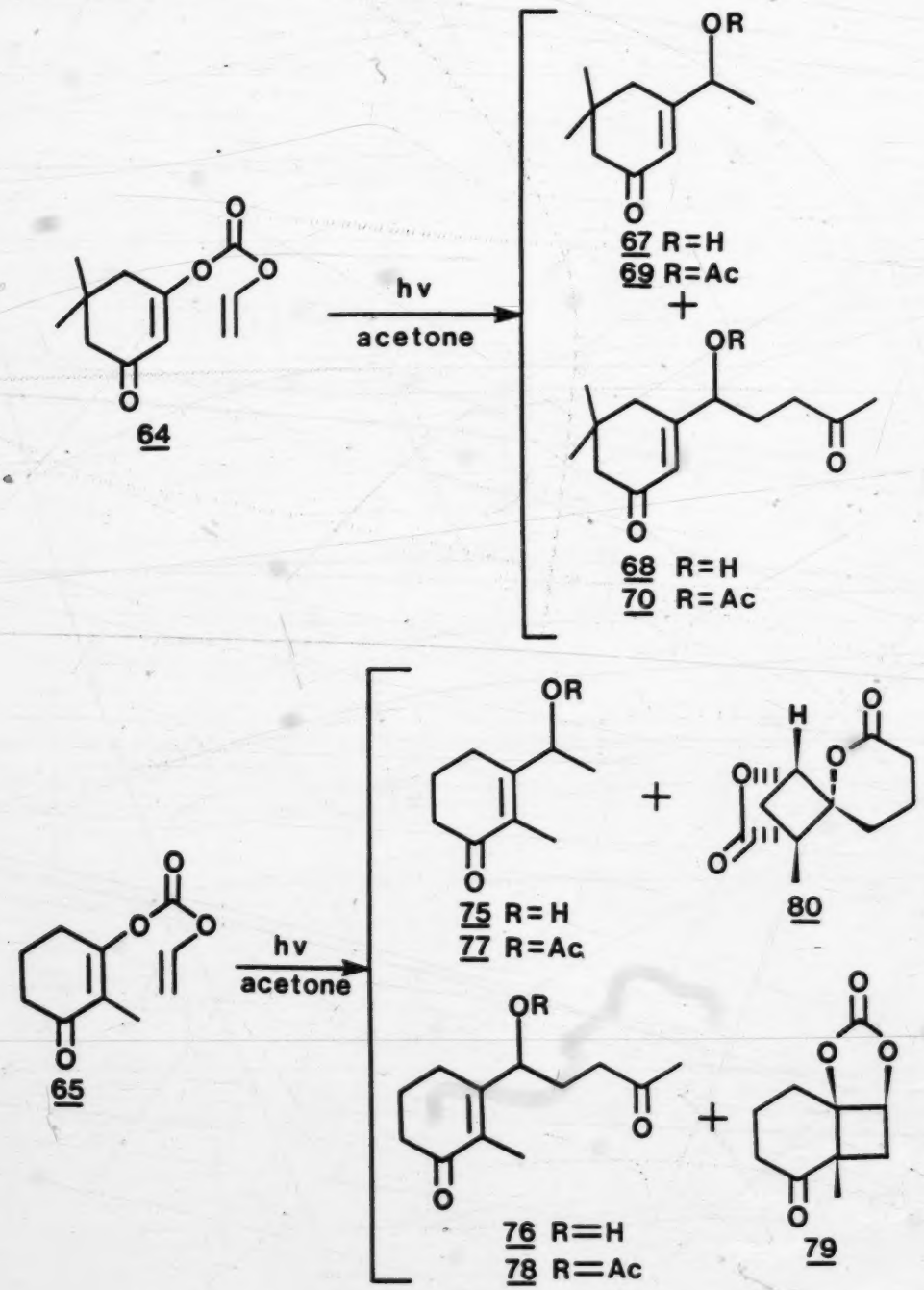
*The photoadduct 66 was photolabile and decomposed to a complex mixture of products if irradiated for a long period of time.

Scheme 6. Photocycloadditions of enones 64 and 65

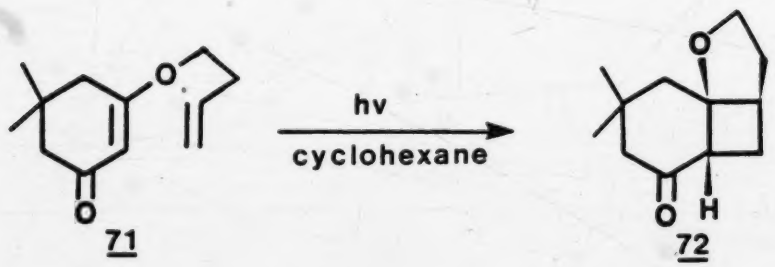


prepared (pyridine, 4-DMAP, Ac_2O) for easier characterization.

The mass spectrum of compound 69 shows a molecular ion at m/z 210.1256 which corresponds to a molecular formula $C_{12}H_{18}O_3$. The ir spectrum of 69 shows absorptions at 1743 cm^{-1}, 1670 cm^{-1}, and 1635 cm^{-1} indicative of an acetoxyl carbonyl and an enone. Its ^1H nmr spectrum shows signals at δ 6.01 (α-vinyl proton of enone), δ 2.09 (acetoxyl methyl), and at δ 1.83 (d, J=6.5 Hz, secondary methyl which is coupled to a low field signal at δ 5.25). These data are consistent with the assignment of structure 67 (from 69) for the first product.

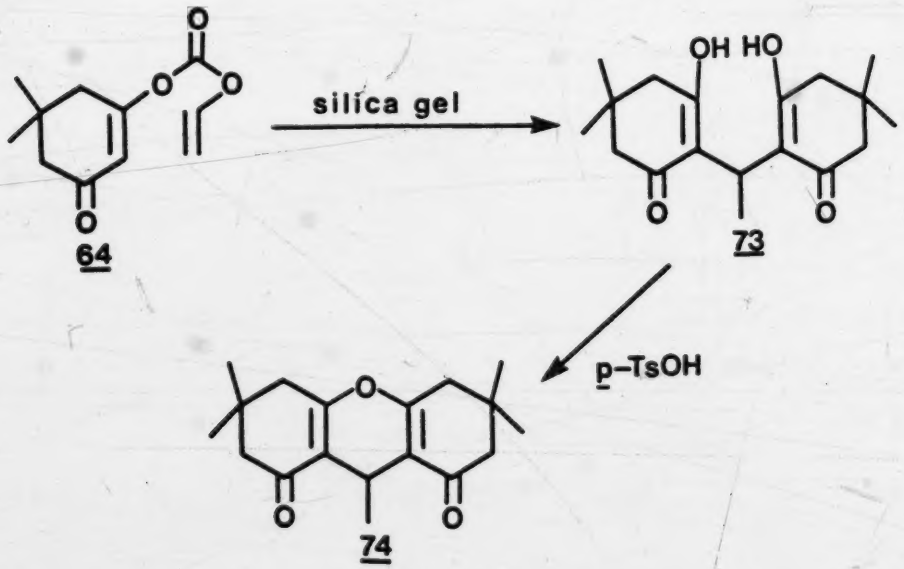
Compound 70 has a molecular ion in the mass spectrum at m/z 266.1518 which corresponds to the molecular formula $C_{15}H_{22}O_4$. This product displays spectral properties similar to those of compound 69. Compound 70 has one acetoxyl group and an enone as evidenced by absorptions at 1745 cm^{-1}, 1671 cm^{-1}, and 1631 cm^{-1} in its ir spectrum and signals at δ 5.97 and δ 2.22 in its ^1H nmr spectrum. The presence of a methyl ketone was suggested by its ir (1717 cm^{-1}) and ^1H nmr (δ 2.16, 3H, s) spectra. These data are consistent with the assignment of structure 68 (from 70) for the second product.

No tricyclic photoadduct was isolated upon irradiation of enone 64. However, irradiation of the structurally similar enone 71 (cyclohexane, Pyrex) gave a 55% yield of photoadduct 72.[31] Enone 64 was found to give diol 73 upon contact with silica gel (Scheme 7). The structure of 73 was confirmed by acid-catalyzed conversion to the known compound 74.[32]



71 72

Scheme 7: Conversion of 64 to 74

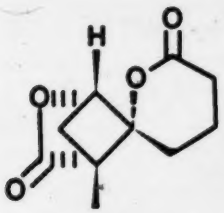


64 73 74

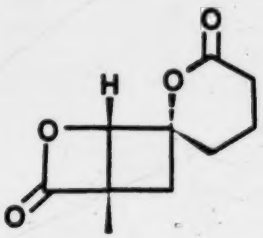
Irradiation of enone 65 under conditions similar to those used in the photolysis of 64 produced four major products. Two of the products were identified as the cyclohexenone derivatives 75 (8%) and 76 (10%) based on examination of the spectral data of their monoacetate derivatives 77 and 78 (vide supra). The mass spectra of the other two products indicated that each was a structural isomer of enone 65. The first product obtained in 16% yield was assigned structure 79 based on absorptions at 1805 cm^{-1} and 1707 cm^{-1} in its ir spectrum and a signal at δ 4.75 (dd, 1H, J=4, 6.5 Hz) in its ^{1}H nmr spectrum.

A second product obtained in 9% yield had absorption at 1797 and 1735 cm^{-1} in its ir spectrum and shows signals at δ 176.3 and δ 168.7 indicative of two lactone carbonyls in the ^{13}C nmr spectrum. The ir absorption band at 1797 cm^{-1} is characteristic of either a β -lactone (1825 cm^{-1})[33] or a γ -lactone (1770 cm^{-1})[34] while the absorption at 1735 cm^{-1} is consistent with a six-membered ring lactone. The ^{1}H nmr spectrum (CD_2Cl_2) of this product together with spin-spin decoupling experiments indicate the presence of three contiguous methylene groups, a methylene group one proton of which is coupled (J=1.5 Hz) to a lower field proton, a methyl group (δ 1.26, s), and a methine proton (δ 4.85, d, J=1.5 Hz) coupled to one proton

of the methylene group. From these data it is possible to propose either structure 80 or 81 for the photoadduct.



80



81

An X-ray crystallographic study of this compound was carried out to distinguish between the two possible structures.* Figure 1 shows a computer generated perspective drawing of the X-ray model of this compound, which reveals that it possesses structure 80. Interestingly, compound 80 exhibits a large four-bond carbon hydrogen coupling constant (J=3.5 Hz)** between the methine proton and the methyl carbon.

The formation of the photodecomposition products 75 and 76 from 65 (and correspondingly 67 and 68 from 64) are rationalized in Scheme 8. Initial bond formation occurs at C-3 of enone 65 to form intermediate biradical 82[37] (in

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*The X-ray crystallographic study (partial refinement) was carried out by R.G. Ball, Structure Determination Laboratory, Department of Chemistry, University of Alberta, Edmonton, Alberta, T6G 2G2. Some details are provided in reference 35.

**Stothers[36] reports a four-bond carbon hydrogen coupling constant of 1.1 Hz for benzene.

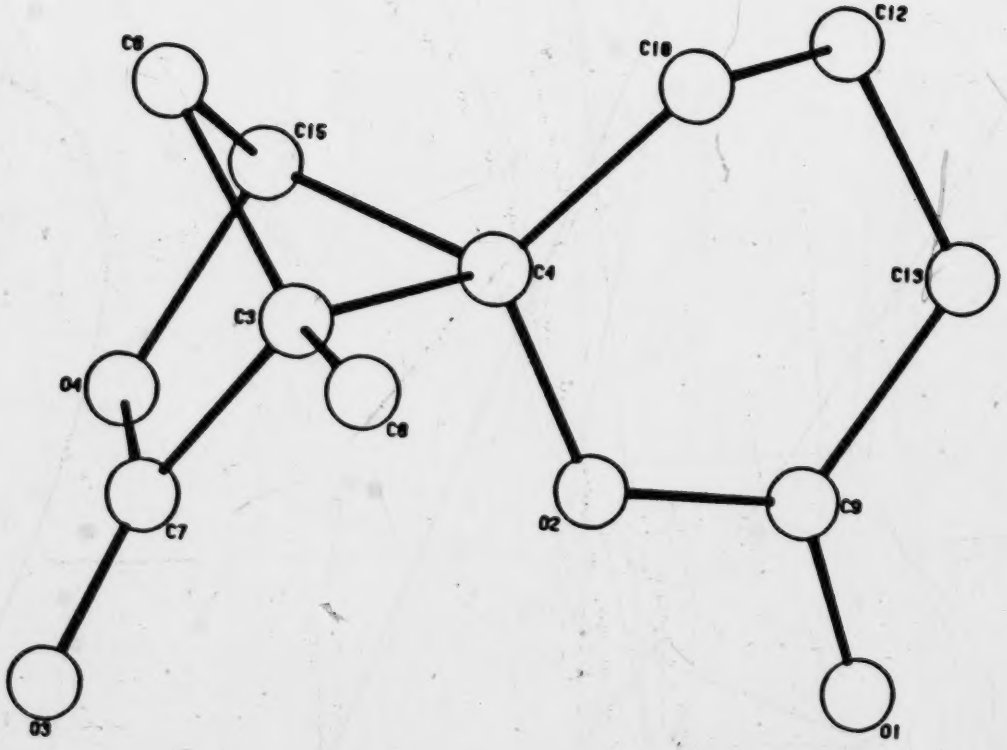
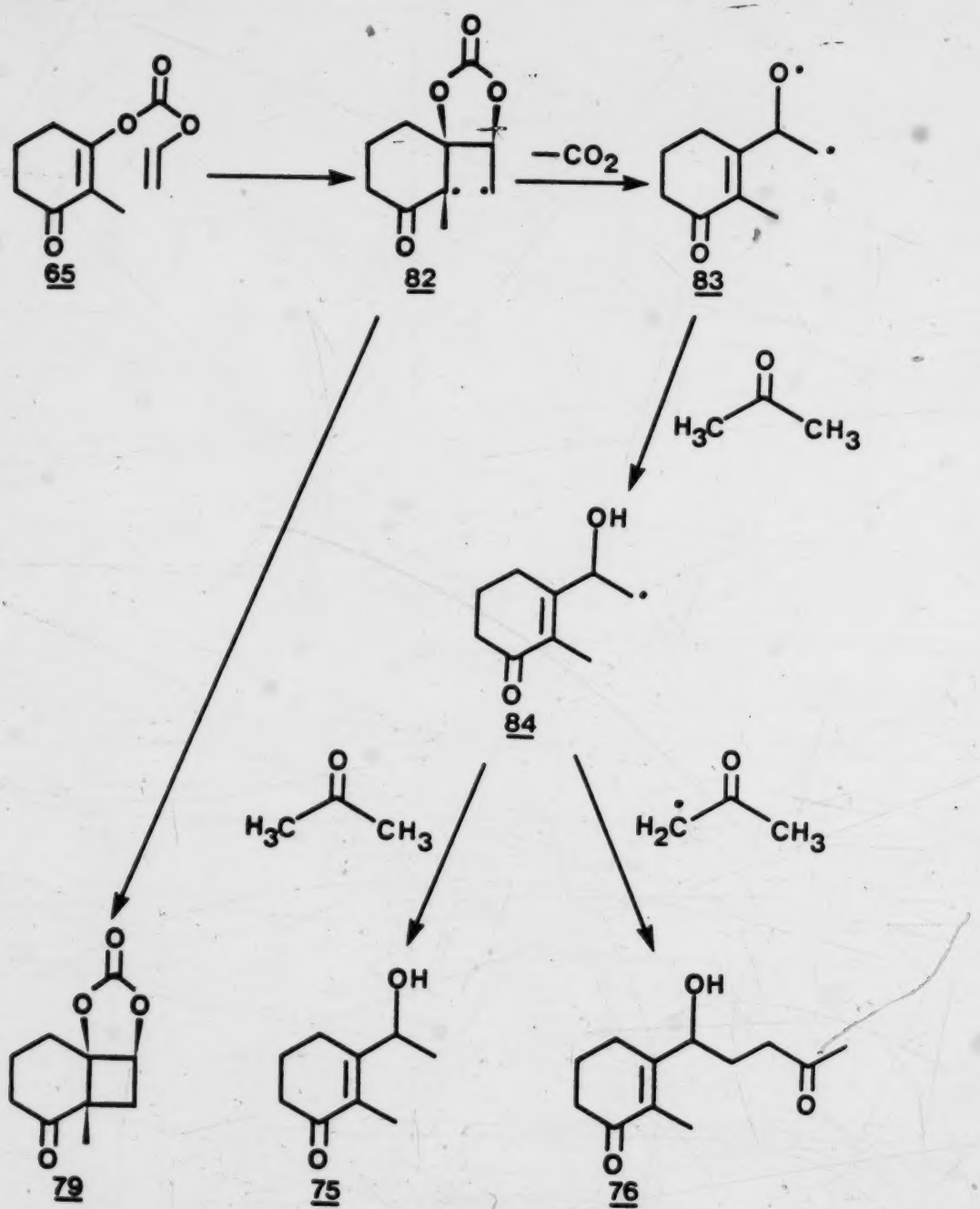


Figure 1. A computer generated perspective drawing of the X-ray model of compound 80. Hydrogens have been omitted for clarity and no absolute configuration is implied.

Scheme 8. Formation of 79, 76, and 75 from enone 65



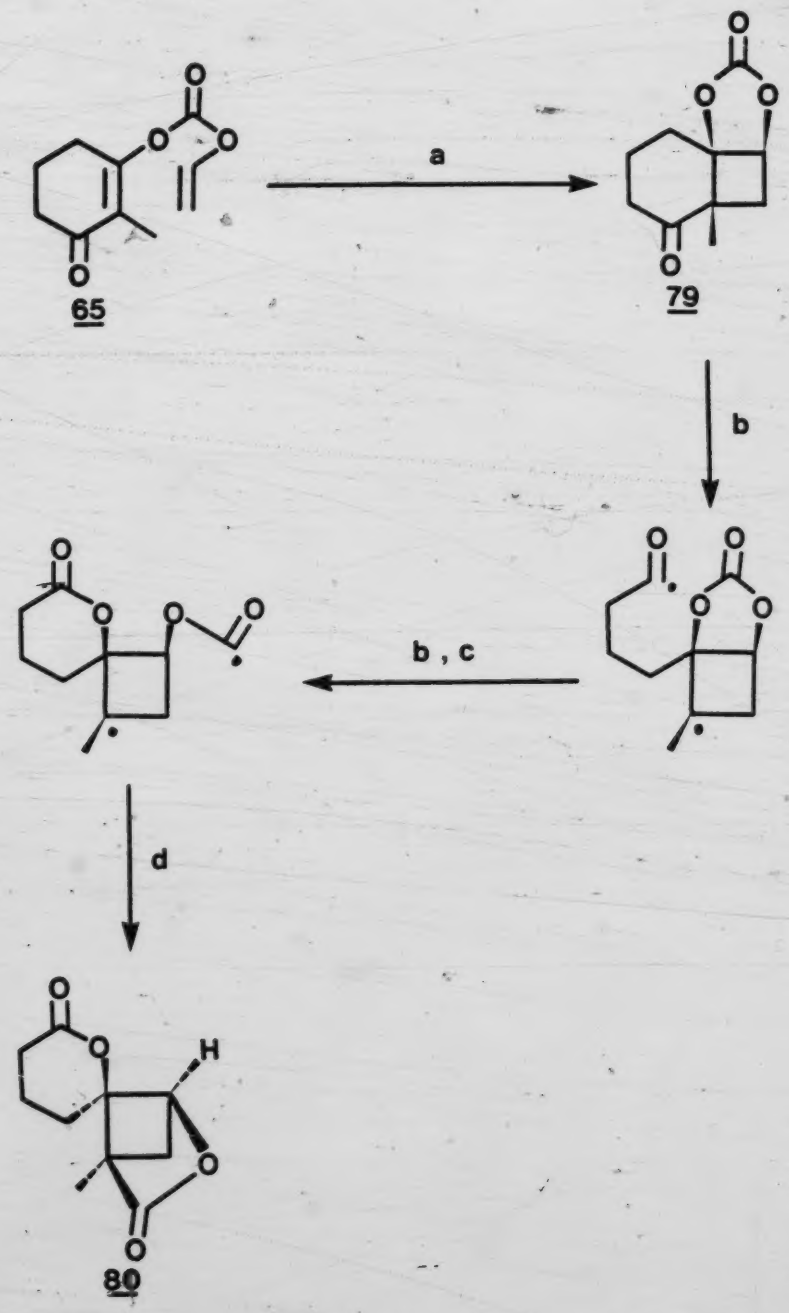
agreement with the rule of five). Biradical 82 can react to give photocycloadduct 79 or can eliminate carbon dioxide to give the biradical 83. Abstraction of a hydrogen atom from a solvent molecule followed by coupling of two radicals (84 and that from solvent) may give rise to 76. Alternatively biradical 83 may abstract two hydrogen atoms from solvent molecules to give 75.

The formation of spiro product 80 may be explained as arising from compound 65 as shown in Scheme 9. Compound 65 undergoes a series of Norrish type 1 cleavages[38] and carbon-oxygen and carbon-carbon bond formations to produce 80.*

Basic hydrolysis of both tricyclic ketones 25 and 66 led to a complex product mixture. However basic hydrolysis (K_2CO_3, aqueous MeOH) of ketone 79 gave diol 85 in quantitative yield. The ir spectrum of 85 shows absorption bonds at 3403 cm^{-1} and 1750 cm^{-1} which indicate the presence of hydroxyl groups and a cyclopentanone respectively. The formation of diol 85 from 79 may be rationalized as shown in Scheme 10.

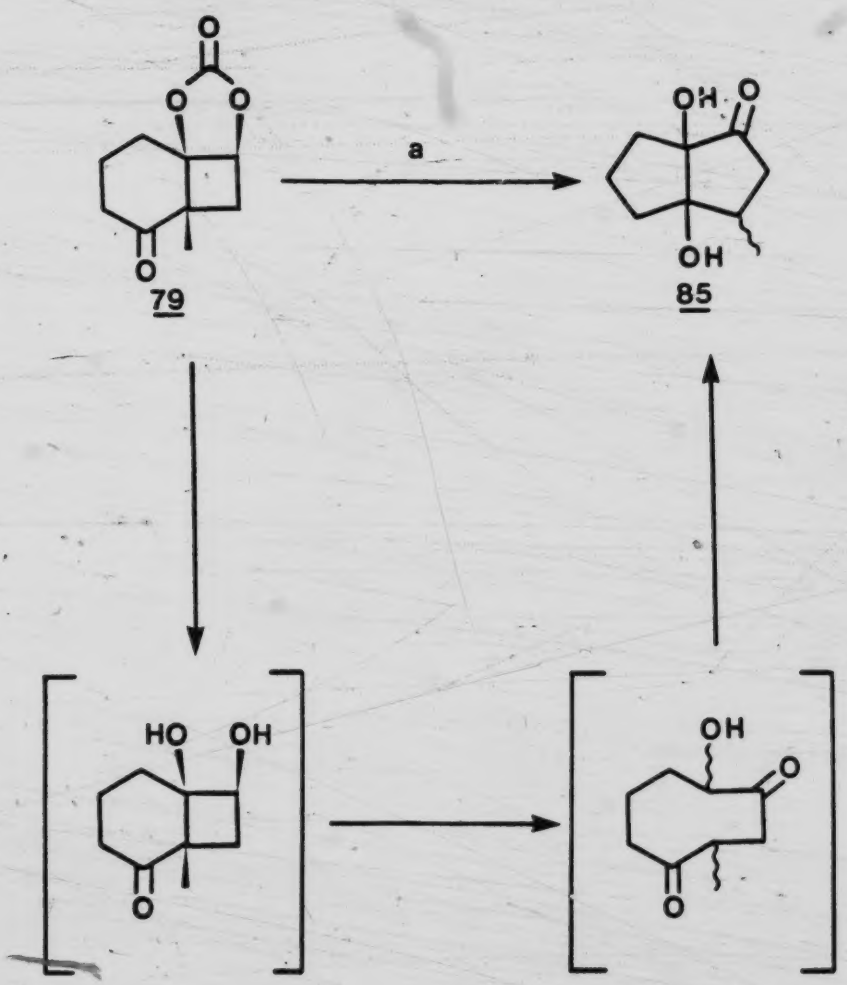
*The control experiment of irradiating 79 to give 80 was not carried out.

Scheme 9. Formation of 80 from enone 65



a) hv b) Norrish type 1 cleavage c) C-O bond formation
d) C-C bond formation.

Scheme 10: Conversion of 79 to 85



a) K_2CO_3, aq. MeOH

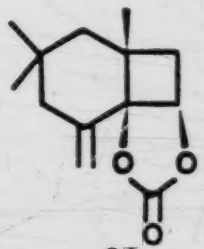
4. Transformation of the Model Bicyclo[4.2.0]compound to a BC Ring Intermediate

After successfully preparing 25 through a photochemical reaction we focused our attention on the conversion of the photoadduct 25 to the target compound 22. Two major problems to be solved in the synthesis of 22 from 25 are the reduction of the C-8 oxygen functionality to the hydrocarbon and the conversion of the C-2 ketone to the desired C-2 vinylic methyl group. Before the deoxygenation sequence was attempted the carbonyl at C-2 was protected, since hydrolysis of 25 leads to a complex mixture of products presumably arising from retro-aldol fragmentation of diol 86.

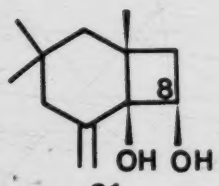
25 86

To circumvent the undesired fragmentation reaction, protection of the carbonyl with different carbonyl protecting groups was investigated. The ethylene acetal of ketone 25 was prepared. However, the product proved to be unstable, rapidly decomposing to a mixture of products. The exocyclic methylene derivative 62 was formed by Wittig

reaction ($Ar_3P=CH_2$) of ketone 25. Compound 62 is stable and it was felt that the exocyclic methylene group could eventually be transformed to the desired vinyl methyl grouping. Compound 62 was hydrolyzed (K_2CO_3, aqueous MeOH) to give the crystalline diol 61 in 86% overall yield from 25.



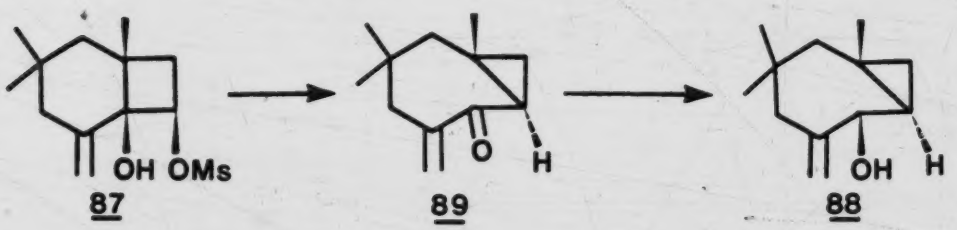
62



61

With diol 61 in hand, we turned our attention to removal of the C-8 oxygen. It is well known that sulfonates of simple alcohols can be reduced to their corresponding hydrocarbons with lithium aluminum hydride[39] or lithium triethylborohydride.[40] Consequently diol 61 was converted to mesylate 87 (MsCl, Et_3N). Compound 87 is unstable at room temperature over long periods of time but may be stored under nitrogen at 5°C for up to six months with no evidence of decomposition. When mesylate 87 was treated with lithium aluminum hydride a new product 88 was obtained. The ir spectrum of 88 shows an absorption at 3595 cm^{-1} characteristic of an alcohol. Its ^1H nmr spectrum displays three mutually coupled one proton

signals at abnormally high field (δ 0.92, δ 0.79, δ 0.73) suggesting that this compound contains a cyclopropane ring. The structure of 88 was confirmed by pyridinium chlorochromate oxidation. The uv spectrum of the oxidation product 89 displays a λmax characteristic of an α,β-unsaturated ketone. Its ^{1}H nmr shows signals characteristic of cyclopropyl protons. The structure of the oxidation product is assigned as that shown in 89.

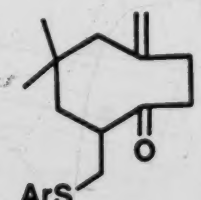


87 89 88

Compound 88 thus has the structure shown. Allylic alcohol 88 presumably arises by pinacol rearrangement of mesylate 87 to enone 89 which is reduced to the alcohol 88 under the reaction conditions. The pinacol rearrangement of similar cis-diols has been shown to proceed stereospecifically to give trans-cyclopropanes.[41] The stereochemistry of the pinacol rearrangement of 87 to 89 will be discussed in greater detail in part 5 of this thesis.

We investigated the displacement of the mesylate group of 87 with other nucleophiles. The ideal nucleophile should be nucleophilic enough to displace the mesylate group but not basic enough to form the tertiary alkoxide. One such nucleophile is the iodide anion. Fujimoto and co-workers[42] have shown that mesylates can be reduced *in situ* with zinc in the presence of sodium iodide to give the hydrocarbon. When mesylate 87 was treated with excess sodium iodide and zinc in dimethoxyethane at 120°C for 4 hours, the rearranged product 89 was obtained as the only detectable product.

Another nucleophile which was investigated was the thiophenoxide anion. This anion is an excellent nucleophile which is not a strong enough base (pKa6-8) to form the alkoxide of a tertiary hydroxyl group (pKa=19).[43] Treatment of mesylate 87 with an excess of sodium thiophenoxide in HMPA at 50°C did not lead to reaction. However upon heating the reaction mixture at 75°C for 17 hours a new, non polar product, compound 90, was formed.



90

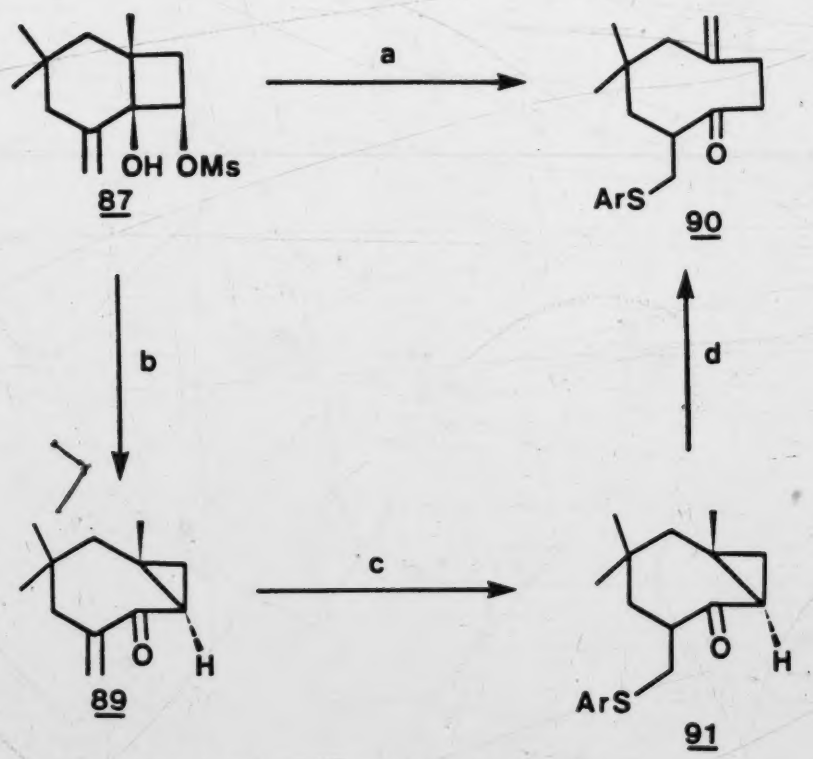
The mass spectrum of 90 shows a molecular ion at m/z 288.1548 which corresponds to a molecular formula of $C_{18}H_{24}SO$. The ^1H nmr spectrum of 90 indicates the absence of mesylate methyl and the presence of a thiophenolate group (δ 7.22, 5H) and an exocyclic methylene group (δ 5.22, 1H; δ 4.94, 1H). On the basis of this and other spectral evidence this compound has been identified as ketone 90.

The formation of compound 90 from 87 was shown to proceed through the intermediates 91 and 92 as indicated in Scheme 11. When mesylate 87 is heated in HMPA at 75°C for 17 hours a loss of methanesulfonic acid with concomitant cyclobutyl ring contraction occurs to yield enone 89. Treatment of enone 89 with lithium thiophenoxide yielded the Michael adduct 91. This adduct could be converted to 90 by treatment with sodium thiophenoxide in HMPA at 75°C for 17 hours. The conversion of 91 to 90 may occur *via* a "retro-ene" type reaction not involving sodium thiophenoxide.

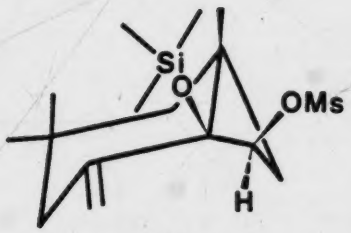
Since hydroxymesylate 87 reacts with nucleophiles to give rearrangement products the tertiary hydroxyl group was protected as its trimethylsilyl derivative 92 (HMDS, TMSCl, DMSO).[44] Reduction of mesylate 92 with either lithium aluminum hydride or lithium triethylborohydride gave diol 61 after aqueous workup indicating that cleavage

of the sulfur-oxygen bond had occurred. These findings are in agreement with the reported observations on the reduction of hindered mesylates.[45]

Scheme 11. Formation of 90 from 87



a. excess ArSNa, HMPA, 75°C, 17 h b. HMPA, 75°C, 17 h
c. ArSLi, THF d. ArSNa, HMPA, 75°C, 17 h



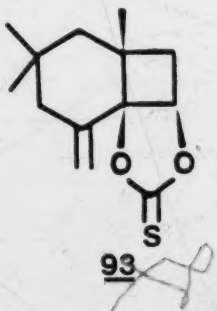
92

It is not completely surprising that nucleophiles such as hydride anion cannot participate in S_n2 displacement reactions at the neopentyl-like C-8 of 92. Displacement would have to take place from the hindered concave face. An attempt was made to invert the C-8 hydroxyl group of 61. In principle, the hydroxyl epimer should be more readily displaced by nucleophiles from the less hindered convex face. Treatment of 61 under Mitsonubi's conditions[46] (Ar_3P, diethyl azodicarboxylate, benzoic acid) led to recovery of cis-diol 61 further emphasizing the hindered nature of the C-8 functionality.

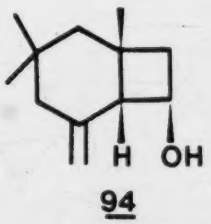
Since the attempts to deoxygenate the C-8 hydroxyl group of diol 61 via its mesylate did not succeed, other methods[47] were explored to achieve this transformation. Barton[48] has demonstrated that thiocarbonylimidazolides derived from the corresponding alcohols are reduced with tributyltin hydride to the corresponding hydrocarbons. It has also been demonstrated that phenoxythionocarbonates[49]

undergo this transformation. The successful application of such a reaction to diol 61 would provide the desired compound.

When diol 61 was treated with either 1,1'-thiocarbonyldiimidazole[21] or chlorophenoxythioformate[49] only the cyclic thionocarbonate 93 was formed. Reduction of thionocarbonate 93 with tributyltin hydride[50] gave alcohol 94. The ^{1}H nmr spectrum of 94 clearly shows a methine signal at δ 2.39 (d, J=7.5 Hz) which is coupled to the hydroxymethine proton at δ 4.14. The ^{1}H nmr data are in agreement with structure 94, indicating that, as expected,[51] the tertiary and allylic carbon-oxygen bond of 93 is cleaved.



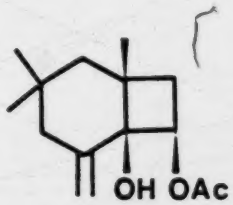
93



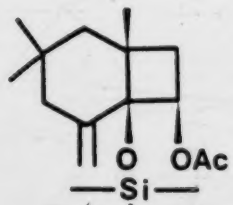
94

Recently it has been reported[52] that the photolysis of acetates at 254 nm in aqueous HMPA effects carbon-oxygen bond cleavage to provide the corresponding hydrocarbon. Acetylation (pyridine, Ac_2O) of the secondary hydroxyl group of 61 gave acetate 95 and protection of the tertiary hydroxyl group as its trimethyl

silyl ether (HMDS, DMSO, TMSCl) afforded the acetate derivative 96. Acetate 96 was dissolved in HMPA containing 5% H_2O and irradiated at 254 nm with a 250-W medium pressure mercury lamp in a quartz immersion well. Unfortunately no reaction occurred. Other attempts to remove the C-8 hydroxyl group of 61 were equally ineffective.



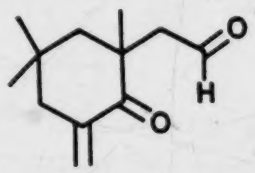
95



96

Since several methods are known for deoxygenation of ketones to the corresponding hydrocarbon, we attempted to oxidize the secondary alcohol of 61 to a ketone. Danheiser has demonstrated[53] that predominant carbon-carbon bond cleavage occurs when diols with a structure similar to 61 are oxidized with a variety of oxidizing agents (Jones and Collins reagents, N-bromosuccinimide, tert-butyl hypochlorite, various Pfitzner-Moffatt type reagents and silver carbonate on Celite). Indeed we found that pyridinium chlorochromate oxidation (buffered with sodium acetate) of diol 61 gives aldehyde 97. Since oxidations involving acidic or basic conditions may cause

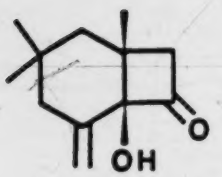
glycol cleavage of 61, we investigated oxidation methods which occur under relatively neutral conditions.



97

Danheiser[53] has further reported that oxidation of sensitive vicinal-diols to the corresponding α -hydroxy ketones can be accomplished in high yields using Swern's oxidation procedure. This oxidation* proceeds rapidly at low temperature and produces relatively innocuous byproducts: carbon monoxide, carbon dioxide, dimethyl sulfide, and triethylamine hydrochloride. Swern oxidation (1.2 eq. oxalyl chloride, 5 eq. DMSO, CH_2Cl_2, -76°C; 5 eq. Et_3N, -76°C) of diol 61 afforded a mixture of four compounds, including ketoalcohol 98 in 89% yield (based on starting material consumed). The ir spectrum of 98 displays an absorption band at 1797 cm^{-1} confirming the presence of the four-membered ring ketone. The other components of the mixture are recovered diol 61 (21%), methylthiomethyl ether 99 (5%) and 100 (5%). Various

*For a review of Swern oxidations see reference 54.



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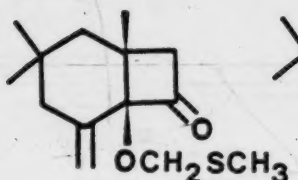

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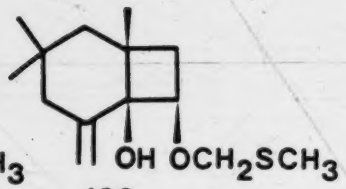
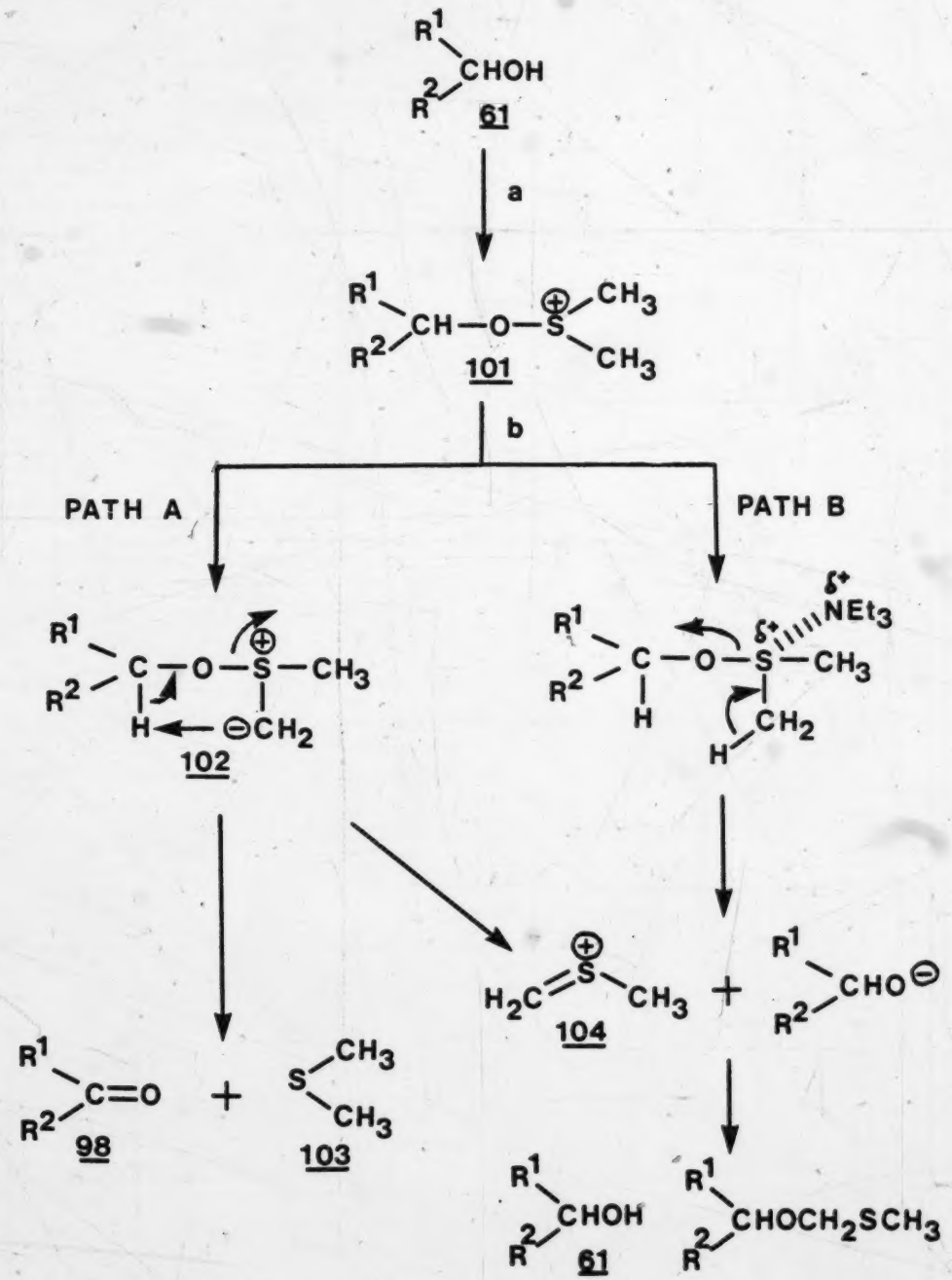


100

attempts to improve the yield of 98 while decreasing the yields of 99, 100, and especially recovered 61, were unsuccessful. For example, when the Swern oxidation of 61 was carried out with excess oxalyl chloride (5 eq.) no diol 61 was recovered. However, the major product was methylthiomethyl ether 99. Other reaction conditions including variation in reaction times, base (diisopropylethylamine instead of triethylamine), or dimethyl sulfoxide activator (trifluoroacetic anhydride instead of oxalyl chloride) did not lead to improved yields of 98. Scheme 12 indicates how the various products arise.[54] The oxidation proceeds through the dimethylalkoxysulfonium salt 101. The base, Et_3N, removes the proton from the methyl group of the salt 101 to form ylid 102 which then collapses to ketone 98 and dimethyl sulfide 103 by an intramolecular hydrogen transfer (path A). Alternatively the base attacks the sulfur atom to give back alcohol 61 and methylsulfonium cation 104 (path B). The methylthiomethyl ethers 99 and 100 are byproducts

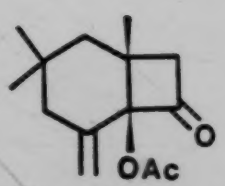
Scheme 12. Swern oxidation of alcohol 61



a. oxalyl chloride, DMSO, CH_2Cl_2, -76°C b. Et_3N, -76°C --> 25°C.

that result from the reaction of the corresponding alcohols with cation 104.

We next explored methods for the transformation of the ketone carbonyl of 98 into a methylene group. Ketoalcohol 98 was converted (Et_3N, Ac_2O, 4-DMAP) to ketoacetate 105 to prevent rearrangement involving the free tertiary hydroxyl group of 98 (vide supra). The Wolff-Kishner and Clemmensen reductions[55] of ketones are conventional methods that employ strongly basic or strongly acidic conditions. Such reactions would be incompatible with the labile acetate functionality as well as the carbon-carbon double bond in compound 105. Thioketal formation followed by desulfurization with Raney nickel[56] is not always a selective method for deoxygenation of ketones in the presence of carbon-carbon double bonds.[57]



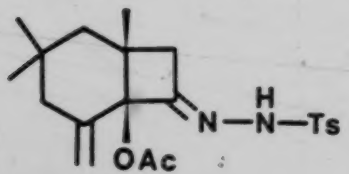
105

A mild, convenient, deoxygenation method involves reduction of the tosylhydrazone derivative with boron hydride reagents followed by decomposition of the

reduction product. One of the most versatile of these procedures involves the use of catecholborane[58] as the reducing agent. This procedure offers a number of advantages over methods utilizing sodium borohydride[59] and sodium cyanoborohydride.[60] The advantages include: (a) only 1 equivalent of hydride is necessary; (b) mild reaction conditions (room temperature, neutral pH, and the use of common aprotic solvents); (c) the inertness of most functional groups towards catecholborane (only aldehydes are reduced more rapidly than tosylhydrazones). Since tosylhydrazone formation does not require acid or base catalysis,[61] this procedure is the method of choice for reducing ketones in compounds that contain other sensitive functional groups.

Ketoacetate 105 was converted (tosylhydrazine, EtOH) to tosylhydrazone 106 in quantitative yield. Compound 106 was reduced (1.4 eq. catecholborane, 0°C, $CHCl_3$; excess NaOAc, DMSO, reflux) to the acetate 26. The mass spectrum of 26 shows a molecular ion at m/z 222.1620 corresponding to a molecular formula of $C_{14}H_{22}O_2$. The ^1H nmr spectrum indicates the presence of four mutually coupled proton signals at δ 2.55, δ 2.33, δ 1.67 and δ 1.35 indicating that the cyclobutane ring is intact in acetate 26. Compound 26 was isolated in low overall yield (26%) from 105. Tlc analysis during the course of the reaction

indicated that the catecholborane had completely reacted with 106 to give one product, presumably intermediate 107.



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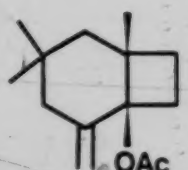

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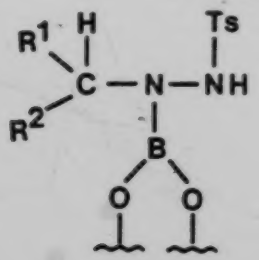
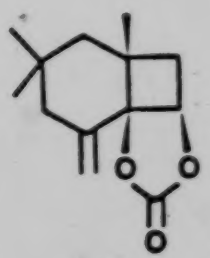


107

Variation of the reaction conditions by treatment with n-Bu_4NOAc instead of NaOAc did not improve the yield of 106. Since Kabalka and workers[58, 62] have reported that the decomposition of an intermediate such as 107 with either NaOAc or n-Bu_4NOAc leads to excellent yields of the corresponding hydrocarbon, we feel that the low yields may be due to the small scale on which we performed the reaction and perhaps the volatility of 26. The volatility problem should not be encountered when the reaction is applied in the total synthesis of sterpuric acid (1).

The last step to be investigated in the synthesis of model compound 22 is the isomerization of the exocyclic double bond to an endocyclic double bond. Because of the volatility and limited amount of 26 available, we investigated the isomerization of the alkene carbonate 62 to carbonate 108. Rhodium(III)chloride trihydrate has been reported to bring about isomerization of exocyclic to endocyclic double bonds.[63] Compound 62 was isomerized to 108 with this reagent [$Rh(III)Cl_3 \cdot 3H_2O$, isopropanol, reflux, 4 days). The ^1H nmr spectrum of 108 shows the vinyl proton signal at δ 5.70. Compound 108 was also formed by treating ketocarbonate 25 with methyllithium to form a tertiary alkoxide. Treatment of this alkoxide with thionyl chloride and pyridine led to alkene 108 in 78% overall yield from ketone 25.



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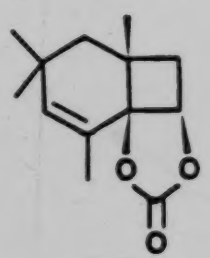


108

The methodology that has been developed in the model studies for the synthesis of 26 and 108 from isophorone (23) should be applicable to the total synthesis of sterpuric acid (1).

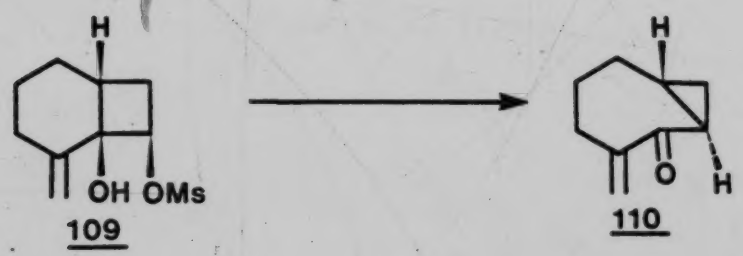
5. Examination of the Pinacol Rearrangement of Bicyclo [4.2.0]octane-1,8-diols

We were intrigued by the pinacol rearrangement of mesylate 87 to cyclopropane 89. Paukstelis and other workers[41] have reported that the reaction of similar cis-hydroxymesylates gives a trans-cyclopropane. Under basic conditions the rearrangement proceeds through formation of the alkoxide of the tertiary hydroxyl group. Collapse of the alkoxide leads to the formation of the ketone with concomitant migration of a carbon-carbon bond and elimination of the mesylate group. A carbon-carbon bond which is trans to the leaving group (for 87 this is the ring junction carbon-carbon bond) is most likely to migrate and a stereospecific rearrangement with retention of configuration at the new ring junction is expected. The formation of the trans-cyclopropane 89 is sometimes difficult to visualize, since the hydrogen on C-8 of 87

87 89

remains on the same face of the molecule. At first glance this does not appear to be an internal S_n2 displacement. However, an S_n2 inversion does occur at C-8 of 87 but the bonds undergoing inversion are a-b and b-c.

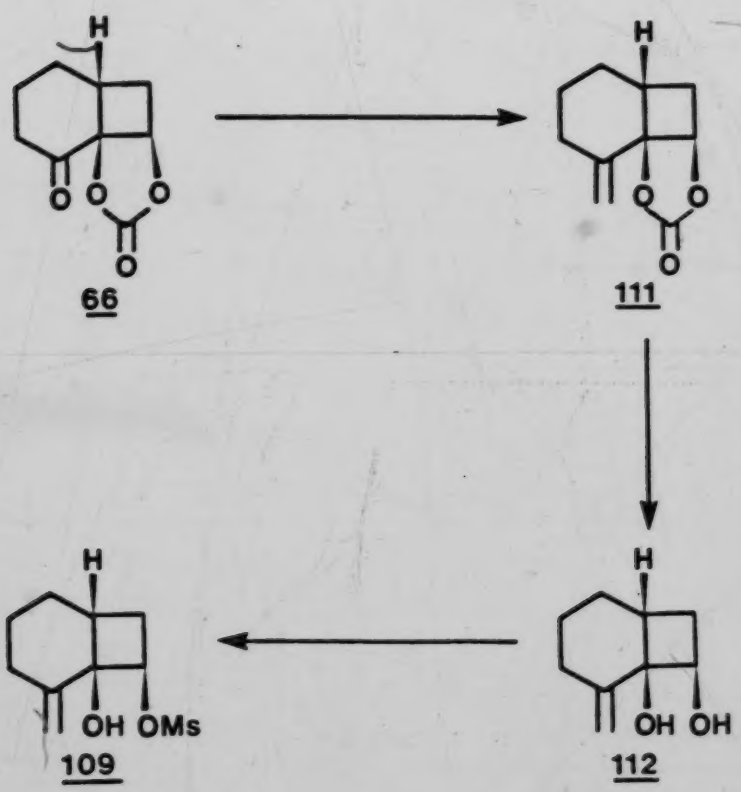
To explore this reaction further and to prove the relative ring junction stereochemistry of 89 we decided to synthesize mesylate 109. This mesylate should undergo the pinacol rearrangement to give trans-cyclopropane 110.



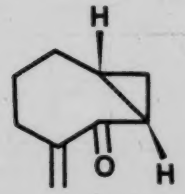
109 110

Comparison of the ^1H nmr coupling constant of the ring junction protons with those reported in the literature should, in principle, allow us to assign the ring junction stereochemistry.

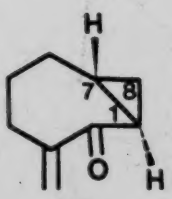
Accordingly mesylate 109 was synthesized following the procedure outlined for mesylate 87 (vide supra). Wittig methenylation ($Ar_3P{=}CH_2$) of ketocarbonate 66 gave alkene carbonate 111 which was hydrolyzed (K_2CO_3, aqueous MeOH) to the cis-diol 112. Mesylation (pyridine, MsCl) of diol 112 afforded crude mesylate 109 which was not sufficiently stable for characterization. Instead the



crude mesylate was immediately passed through a column containing basic aluminum oxide to afford mainly trans-cyclopropane 110. The ^{1}H nmr spectrum of the product indicates that a small amount (ca. 3%) of the corresponding cis-isomer 113 is also present. This isomer could not be separated from the trans-isomer 110 but is conveniently separated in subsequent steps. The presence of the cis-isomer did not hinder the spectral assignment of the trans-cyclopropane 110.



113



110

Double irradiation experiments reveal that the signal at δ 0.07 (dddt, J=2.8, 6.5, 11.5, 7.5 Hz) in the ^{1}H nmr of 110 may be assigned to H-7. It is not possible to unequivocally assign the signals for H-1 and the two H-8 protons. Each of these ^{1}H signals appears as a doublet of triplets with coupling constants ranging from 5.5 to 7.5 Hz. Lanthanide induced shift (LIS)[64] experiments with Eu(fod)$_3$* were considered as a possible aid in the assignment of the signals in the ^{1}H nmr of 110. The lanthanide shift reagent should bind to the C-2 ketone thus causing the H-1 resonance to undergo a larger shift per increment of shift reagent than the two H-8 signals. However, lanthanide shift reagent studies showed that two of the three ^{1}H signals in question experienced similar large chemical shifts in the ^{1}H nmr so no firm conclusions could be drawn.

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*Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato) europium. Aldrich Chemical Company, Inc.

The H-1 signal was readily assigned from selective proton heteronuclear decoupling experiments (SPD) after the multiplicities of all the ^{13}C signals were determined from gated spin-echo experiments (GASPE).[65] For example, the GASPE experiment with enone 110 established the presence of two methine carbon signals at δ 32.0 and δ 25.5 which are assigned to C-1 and C-7. SPD at δ 0.07 (H-7) results in marked sharpening of the carbon resonance at δ 32.0 allowing identification of this signal as C-7. Thus, by exclusion, the resonance at δ 25.5 must be C-1. SPD of the signals for H-1 and the two H-8 protons demonstrates that only irradiation of the signal at δ 1.31 is accompanied by a marked sharpening of the carbon resonance at δ 25.5. This shows that H-1 resonates at δ 1.31 and that the signals at δ 1.57 and δ 0.88 correspond to the two H-8 protons.

Double irradiation of the signals corresponding to H-7 (δ 0.07) and H-1 (δ 1.31) shows that the coupling constant between these protons is 7.5 Hz. Jackman and Sternhell[66] report the ranges for vicinal coupling constants of cyclopropane derivatives as:

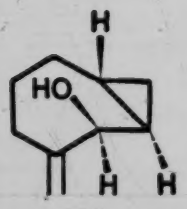
$$J_{cis} = 7.0 - 12.6 \text{ Hz}$$

$$J_{trans} = 4.0 - 9.6 \text{ Hz}$$

Since 7.5 Hz falls in the overlap region for J_{cis} and J_{trans} the ring junction stereochemistry of 110 could not be readily assigned on the basis of coupling constants.

Nuclear Overhauser enhancement difference spectroscopy (nOeds)[67] is a method for determining the relative stereochemistry of substituents in a molecule. A nOeds study of compound 110 was undertaken. Presaturation at δ 0.07 (H-7) reveals no observable nOe enhancement at δ 1.31 (H-1). This result, however, does not prove conclusively the stereochemistry at H-1 and H-7 in compound 110. The cis-isomer, compound 113, may show 0% nOe.

Since the stereochemistry of 110 could not be determined with certainty a crystalline derivative of 110 was prepared for an X-ray crystallographic study. Enone 110 (a liquid) was reduced ($NaBH_4$, $CeCl_3$) to alcohol 114 which then was converted (PhNCO) to the phenylurethane 115. An X-ray crystallographic study of 115 has been



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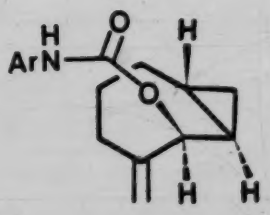

115

carried out.* Figure 2 shows a computer generated perspective drawing of the X-ray model of this compound, which reveals that the stereochemistry of the ring junction hydrogens of 115 (and thus of 110) is trans.

Some of the cis-isomer, compound 113, was formed during the pinacol rearrangement of mesylate 109. Presumably compound 113 arises by isomerization of trans-compound 110. Since it was not possible to separate the cis-isomer 113 from the trans-isomer 110 by column chromatography, we decided to convert the trans-isomer 110 to the cis-isomer 113. This would allow us to determine the ^{1}H nmr coupling constant for the ring junction protons. Literature reports suggest that the coupling constant Jcis of 113 should be larger than coupling constant Jtrans of 110 (vide supra).[66]

Isomerization of trans-110 by passage through a column containing basic alumina oxide was not successful. Paukstelis[41a] reports that treatment of trans-bicyclo[4.1.0]hexanone (116) with potassium tert-butoxide in tetrahydrofuran gave cis-bicyclo[4.1.0]hexanone 117. However when compound 110 was treated with potassium tert-butoxide a mixture of non uv active compounds was formed.

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*The X-ray crystallographic study (partial refinement) was carried out by R.G. Ball, Structure Determination Laboratory, Department of Chemistry, University of Alberta, Edmonton, Alberta, T6G 2G2. Some details are provided in reference 68.

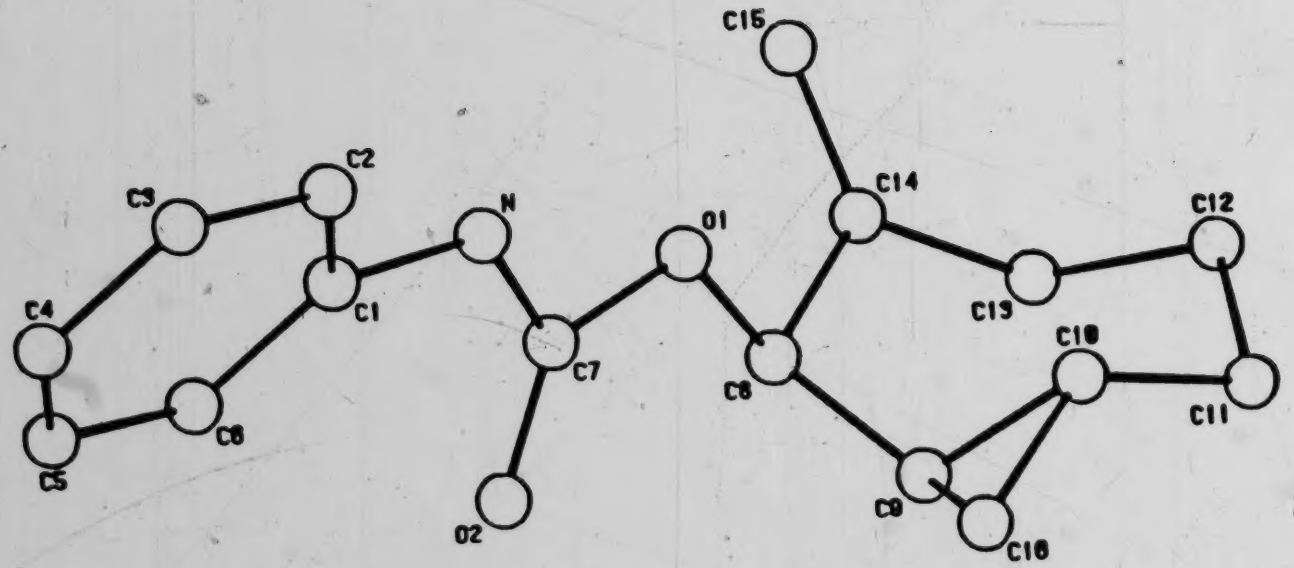
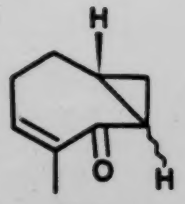


Figure 2. A computer generated perspective drawing of the X-ray model of compound 115. Hydrogens have been omitted for clarity and no absolute configuration is implied.

116 117

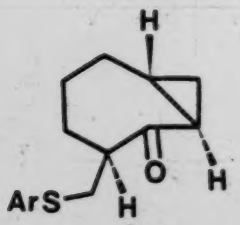
This mixture was not analyzed. Treatment of compound 110 with excess lithium diisopropylamide (>10 eq.) resulted in the formation of two new uv active compounds along with unreacted starting material. A ^{1}H nmr analysis of the crude reaction mixture in the region δ 4-6 indicated that one of the products may be the cis-isomer 113 while the other may be a compound such as 118 with unknown ring junction stereochemistry. However it was difficult to separate compound 113 from the reaction mixture.



118

Since it was difficult to isomerize the trans-isomer 110 completely to the cis-isomer 113 we attempted to prepare derivatives which could be separated. Treatment of compound 110 containing small amounts of cis-113 with

thiophenol and pyridine gave three compounds which were separable by column chromatography. ^{1}H nmr and mass spectral analysis of the products indicated that the three compounds are isomers. The ^{1}H nmr spectrum of the minor compound (3.5% yield) shows a coupling constant between H-1 and H-7 of 10.5 Hz. Since this coupling constant is larger than 7.5 Hz this compound is assigned structure 121 with a cis-ring junction. The ^{1}H nmr spectra of the two major compounds (54% yield, 1:1) were found to have coupling constants of 7.5 and 8.0 Hz between the bridgehead protons H-1 and H-7. This indicates that these two products have a trans-ring junction and thus structures 119 and 120 were assigned to these products. These structural assignments were supported by nOe experiments. Compound 121 shows an nOe enhancement (13%) of the H-1 signal when the H-7 ^{1}H nmr signal is presaturated.



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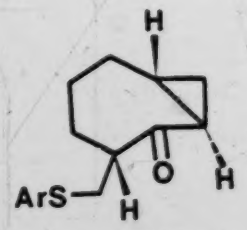

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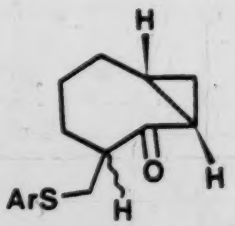
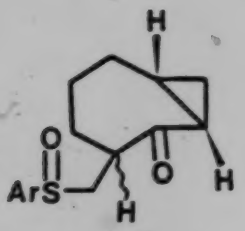


121

Compound 121 was converted to cis-enone 113 in two steps. Treatment of 121 with one equivalent of m-chloroperbenzoic acid gave sulfoxide 122. A solution of 122 in benzene was heated under reflux to give cis-isomer 113. In the ^1H nmr spectrum the coupling constant between H-1 and H-7 of 113 was determined to be 9 Hz. As expected this value is larger than the 7.5 Hz observed for the trans-isomer 110. NOe studies on 113 further confirmed the cis stereochemistry of the ring junction protons.



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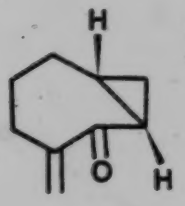
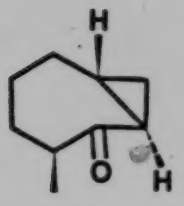


113

The cyclopropane ring of trans-compounds 119 and 120 can be cleaved regiospecifically with Raney nickel. Thus an epimeric mixture (1:1) of 119 and 120 was reacted with excess Raney nickel (W2 grade, ArH, 8 hours, r.t.) to give methyl ketones 123 and 124. If the reaction is allowed to proceed for a longer time (16 hours) then a epimeric mixture (1:1) of cycloheptanones 125 and 126 is obtained in 67% overall yield from 119 and 120. The ^1H nmr spectrum of the mixture of 125 and 126 shows 4 methyl doublets (δ 1.07, δ 1.05, J=7 Hz and δ 1.00, δ 0.98, J=6

Hz) indicating that the cyclopropane bond which is coplanar to the carbonyl π bond was cleaved. This result is in agreement with literature reports.[69]



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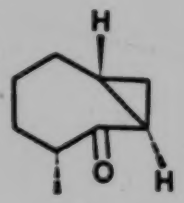

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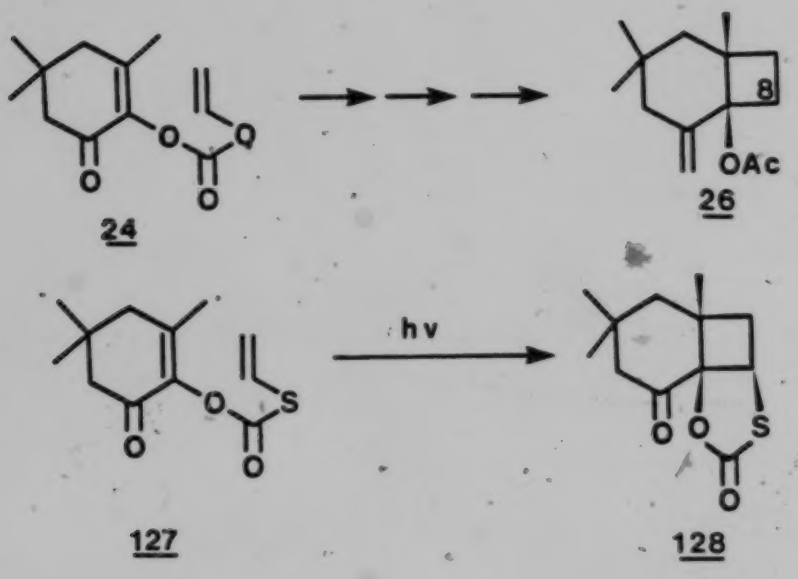
126

6. Formation and Transformation of a 2-[(2-Thiabut-3-enoyl)oxy]cyclohex-2-enone .

The synthesis of the BC ring intermediate 26 requires seven steps from enone 24. Since five of the seven steps are involved with the removal of functionality at C-8, we decided to look at alternative methods for the formation of this compound. One such method involves the use of the vinylthiocarbonate derivative 127. Compound 127 should

undergo a [2+2]intramolecular photocycloaddition reaction* in a manner similar to that of enone 24 to give thiocarbonate 128. Raney nickel desulfurization of 128 should lead directly to the desired compound that has a C-8 methylene group.



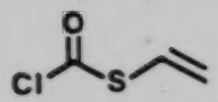
24 26

127 128

By analogy with the formation of enone 24 the most direct approach to 127 involves the reaction of alcohol 31 with S-vinyl thiolchloroformate 129. A search of the literature revealed that 129 has not been reported previously. However, we felt that application of the chemistry employed for the formation of vinyl

*For similar cycloadditions involving vinylthio groups see reference 70

chloroformate 57 should be applicable to the synthesis of 129.

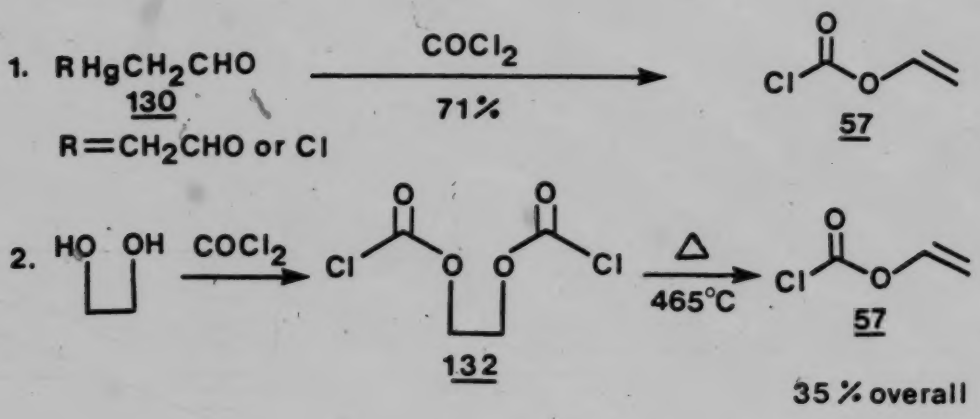


129

Two methods for the preparation of 57 are shown in Scheme 13. Method 1, which involves the reaction of mercuro compound 130 with phosgene, is the industrial procedure currently used for the formation of vinyl chloroformate.[71] The application of this method towards the preparation of 129 would involve the preparation of thioaldehyde 131. Thioaldehydes are notoriously unstable molecules which readily polymerise;[72] the first stable thioaldehyde, 2,4,6-tri-t-butylthiobenzaldehyde was synthesized three years ago by Okazaki and coworkers.[73]

Another method for the formation of 57 involves the gas phase pyrolysis of bischloroformate 132.[74] The pyrolysis is reported to proceed via a one-step unimolecular mechanism (Ei mechanism) through a cyclic transition state. By analogy the sulfur analogue 133

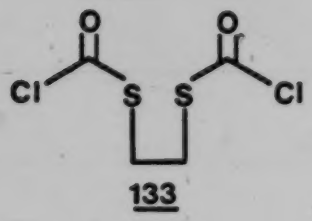
Scheme 13. Two methods for the preparation of 57



$RHgCH_2CHS$

131

should undergo a similar pyrolysis reaction to give 129. Accordingly the bisthiolchloroformate 133 was synthesized from ethanedithiol (pyridine, $COCl_2$). It was subjected to pyrolysis and the reaction products were analyzed by ^1H nmr spectroscopy. Pyrolysis at temperatures up to 450°C caused some decomposition of 133 along with the formation of thiocarbonate 134. When the pyrolysis was carried out at 515°C some 129 was formed (<3%) as evidenced by ^1H nmr



133

134

signals (80 MHz) in the reaction product at δ 6.75 (dd, J=10, 17 Hz), δ 5.57 (d, J=17 Hz), and δ 5.54 (d, J=10 Hz). At this temperature extensive decomposition of 133 occurred, and small amounts of compound 134 (<17%) were formed. Unfortunately, pyrolysis conditions could not be developed which gave improved yields of 129. Since compound 133 undergoes extensive decomposition* at these temperatures this method of preparation of compound 129 was discontinued.

Compound 129 may be prepared by reaction of the vinylthioanion 135 with phosgene. Olofson,[71b] however, was unable to prepare vinyl chloroformate by acylation of the enolate of acetaldehyde with phosgene. The lack of success may be due to the ambidentate nature of the enolate and/or the reaction of the enolate forming base and its conjugate acid with phosgene and the desired product. The thioanion 135, however, would be expected to acylate exclusively on sulfur. Since thioacetaldehyde 136 is not stable and polymerises readily[72] other precursors to 135 were investigated.**

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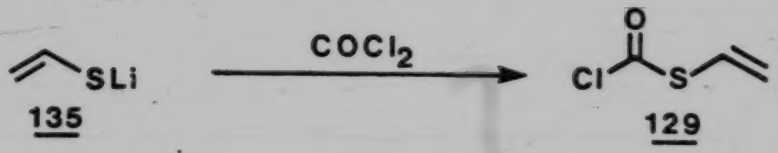
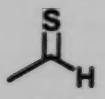
*Thaler[75] has synthesized 133 by a different route. Attempted purification of 133 by vacuum distillation led to decomposition.

**See reference 76 for different approaches towards the synthesis of thioanion 135.

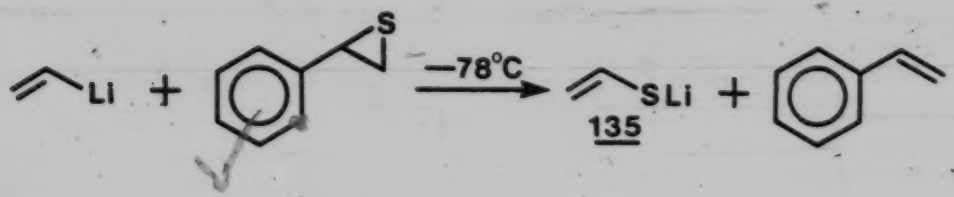


135 129

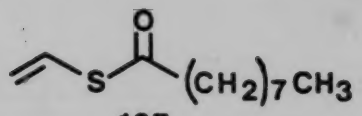


136

Corey[76c] has developed a procedure for the formation of thioanion 135 which involves reacting vinyl lithium (1 eq.) with styrene sulfide (1.5 eq.) at -78°C. Compound 135 reacts with acid chlorides to form vinyl thiolesters. Thioanion 135 was prepared according to Corey's procedure[76c] and was treated with nonanoyl chloride to give 137. The ^1H nmr spectrum of this product indicates the presence of the vinylthio group as evidenced by signals at δ 6.90, δ 5.50, and δ 5.47. The ir spectrum of 137 shows an absorption band at 1710 cm^{-1} indicative of a thiolester.[77]

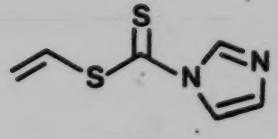


135



137

Unfortunately, when compound 135 was treated with excess phosgene at -78°C no 129 could be isolated after distillation of the reaction mixture. All products isolated which showed an ir absorption characteristic of a thiolester also showed the presence of phenyl substituents in the ^1H nmr spectra. This result indicated that styrene sulfide and/or styrene had reacted with the phosgene. Since phosgene was too reactive an electrophile for our purpose, thioanion 135 was treated with an excess of the less reactive 1,1'-thiocarbonyldiimidazole[21] with a view to preparing either 138 or 139. However, ^1H nmr analysis of the crude reaction mixture did not indicate the presence of the vinylthio group. Since 129 or similar



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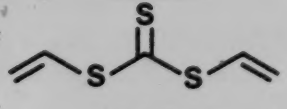
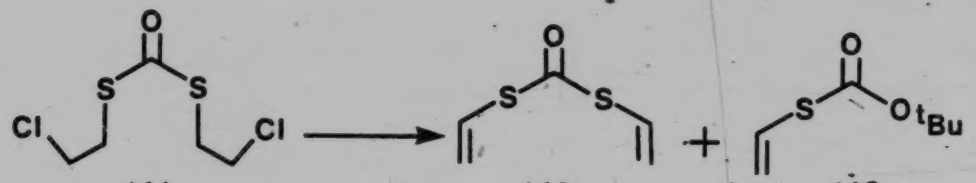


139

derivatives could not be prepared by this method, this line of research was not pursued further.

Treatment of alcohol 31 with S,S'-divinyl dithiocarbonate 140 could conceivably give compound 127 directly. Reagent 140 is formed in low yields (<20%) by reacting dichloro compound 141 with potassium tert-butoxide according to the reported procedure.[78] Attempted formation of compound 140 led to polymerization when purification was attempted using a spinning band column. However, compound 140 was isolated along with compound 142 upon rapid vacuum distillation through a Vigreux column.

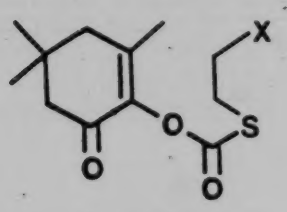


141 140 142

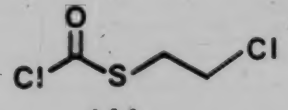
Treatment of alcohol 31 with a 1:1 mixture of 140 and 142 in the presence of either Et_3N or pyridine did not produce the desired vinylthiocarbonate derivative 127. In the presence of Et_3N (DMSO, 45°C) 140 and 142 polymerised, an observation that has been reported previously.[77] When alcohol 31 was treated with sodium or potassium hydride, the corresponding metal salts of 31 were formed. These salts were treated with the mixture of 140 and 142, at 0°C

in THF to give impure 127. Compound 127 could not be separated from a mixture of unidentified products. That 127 had formed was indicated by the ^1H nmr spectrum of the reaction mixture. The spectrum shows the presence of a vinyl proton (δ 6.54, dd, J=10, 17 Hz) and the mass spectrum shows a molecular ion at m/z 240.0820 corresponding to the molecular formula $C_{12}H_{16}O_3S$. This method of preparation of compound 127 gave very low yields (<5%, ^1H nmr) of impure product and thus another route to compound 127 was sought.

Since compound 127 could not be formed directly we attempted to prepare precursors of 127. One suitable precursor is the chlorothiolcarbonate 143 which may be transformed to compound 127 by elimination of HCl.



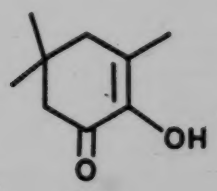
143 X=Cl
145 X=I



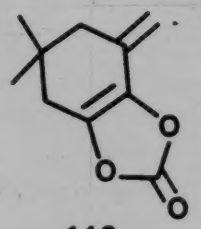
144

Compound 143 was prepared by treating alcohol 31 with S-(β-chloroethyl)chlorothiolformate 144.[78, 79] Since iodide is a better leaving group than chloride the corresponding iodothiolcarbonate 145 was prepared via a

Finkelstein reaction[80] (NaI, methyl ethyl ketone, reflux) of compound 143. Elimination of HCl or HI from compounds 143 or 145, respectively, to form compound 127 was attempted using a variety of bases. Several bases including K_2CO_3,[81] Et_3N,[82] DBN,[83] DBU,[84] and KO^tBu[85] have been successfully employed to effect elimination of a halogen to a sulfur. Unfortunately, treatment of compounds 143 or 145 under a variety of conditions did not lead to the formation of compound 127; alcohol 31, carbonate 146, and/or carbonate 147 were the only reaction



31



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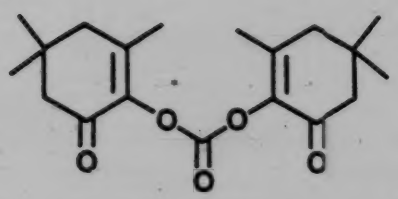
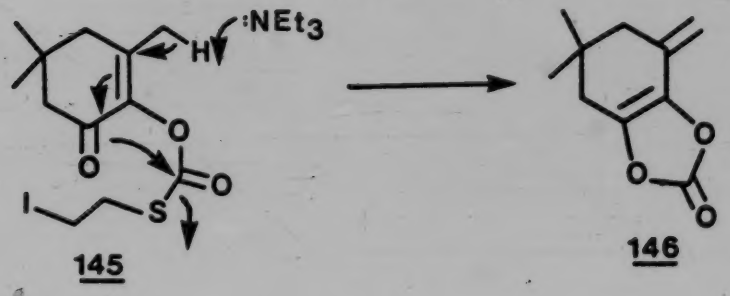


147

products formed. For example, treatment of iodothiolcarbonate 145 with Et_3N (DMSO, 70°C) resulted in the formation of carbonate 146. The structure of

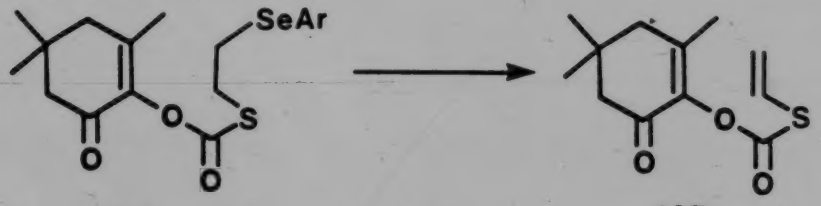
carbonate 146 was assigned on the basis of its mass spectrum which showed a molecular ion at m/z 180.0785 ($C_{10}H_{12}O_3$) and its ir spectrum which showed a carbonate absorption band at 1820 cm^{-1}. The formation of carbonate 146 is rationalized in Scheme 14. Treatment of chlorothiolcarbonate 143 or iodothiocarbonate 145 with KO^tBu in THF or DME resulted in alcoholsis of the thiolcarbonate to give the starting alcohol 31. When compounds 143 or 145 were treated with the hindered bases, DBU or DBN, a mixture of alcohol 31, carbonate 146, and carbonate 147 was formed. Carbonate 147 may arise by reaction of alcohol 31 with either of compounds 143 or 145.

Scheme 14. Formation of carbonate 146 from iodide 145



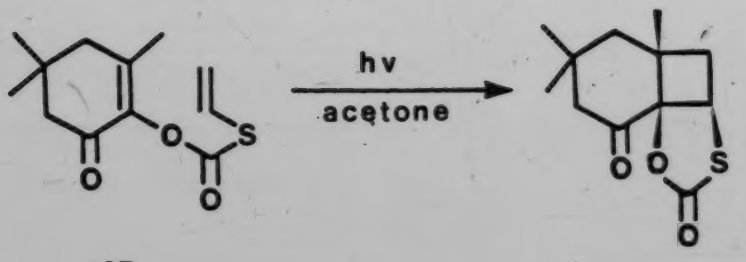
145 146

An alternative method to effect elimination of the halogen in compounds 143 or 145 is by treatment with a nucleophile which can then be modified further before conversion into compound 127. One such nucleophile is selenophenoxide since oxidation of the seleno group to the corresponding selenoxide followed by elimination would lead to the desired intermediate 127.[86] Treatment of sodium phenylselenide (NaH, ØSeSeØ, THF)[87] with iodide 145 at -78°C led to formation of selenide 148 in 92% yield. Oxidation of selenide 148 with hydrogen peroxide (pyridine, CH_2Cl_2, 0°C)[88] led to thioalkene 127 in 62% yield. The vinylthio group was present as evidenced by signals at 6.72 (dd, J=10, 17 Hz), 5.531 (d, J=10 Hz) and 5.528 (d, J=17 Hz) in the ^1H nmr spectrum of 127.



148 127

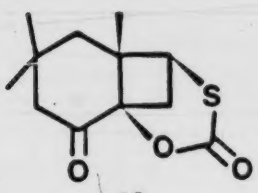
With compound 127 in hand its photolysis was investigated. Compound 127 was found to be more reactive than the corresponding oxygen analogue 24. Photolysis of 127 [200-W medium pressure mercury lamp, 3 Pyrex filters ca. 4.5 mm total thickness, acetonitrile] led to ketothiol-



127 128

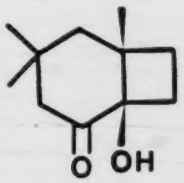
carbonate 128 in 84% overall yield. If a single Pyrex filter (λ >285 nm, ca. 1.5 mm thick) is used the photolysis proceeds more quickly but lower yields of photoadduct 128 are obtained (in the case of 450-W medium pressure mercury lamp the reaction is complete in 10 min). Photolysis of 127 in acetone with a 450-W medium pressure mercury lamp through a Uranium glass filter (λ >333 nm, ca. 1.5 mm thick) led to 74% overall yield of 128.

The identity of ketocarbonate 128 was established by examination of its ir and ^{1}H nmr spectra: ir absorptions at 1732 cm^{-1} and 1705 cm^{-1} and a ^{1}H nmr signal at δ 4.37 (t, J=7.5 Hz, 1H) are especially diagnostic. Since the photocycloaddition of the corresponding oxygen analogue 24 gave the five-membered ring carbonate 25, the corresponding thiocompound 127 is presumed (in agreement with the rule of five[27b]) to give the five-membered ring carbonate 128 rather than the six-membered ring carbonate 149. However the spectral data do not rule out the latter structure.

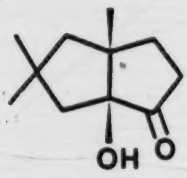


149

We then focused our attention on the reductive removal of sulfur from compound 128. Treatment of compound 128 with Raney nickel resulted in the formation of the desired 150 (27%) and the undesired rearrangement product 151 (30%).



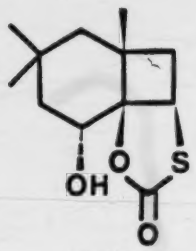
150



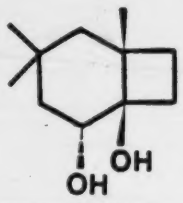
151

The mass spectra of compounds 150 and 151 both show molecular ions at m/z 182.1307 which correspond to the molecular formula $C_{11}H_{18}O_2$. Compound 151 was identified by its ir absorption at 1754 cm^{-1} characteristic of a five-membered ring ketone while compound 150 has an ir absorption at 1736 cm^{-1}. Presumably bicyclo[4.2.0] 150 is formed initially and is partially rearranged to the more stable bicyclo[3.3.0] 151. To prevent this rearrangement

ketone 128 was reduced (sodium borohydride) to alcohol 152. Raney nickel desulfurization of alcohol 152 gave



152



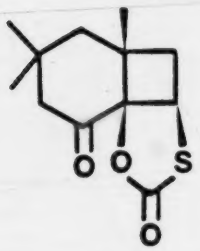
153

diol 153 in 74% overall yield from 128. The mass spectrum of compound 153 shows a molecular ion at m/z 184.1468 corresponding to a molecular formula $C_{11}H_{20}O_2$. The ^1H nmr spectrum of 153 indicates the presence of four mutually coupled proton signals at δ 2.03 (2H), δ 1.67, and δ 1.41 indicating that the cyclobutane ring is intact.

Compound 128 has been converted to compound 22 in three steps. Treatment of ketone 128 with methyllithium (-78°C, THF) followed by dehydration ($SOCl_2$, pyridine) of the resultant tertiary alcohol gave alkene 154. Raney nickel desulfurization of alkene 154 gave alcohol 22 in 68% overall yield from compound 128. The ^1H nmr spectrum of 22 indicates the presence of four mutually coupled proton signals at δ 1.96 (2H), δ 1.69, and δ 1.30, indicating that the cyclobutane ring is intact. The expected cis relationship of the hydroxyl group at C-1 to the methyl group at C-6 is supported by the large pyridine

shift[22] ($\delta CDCl_3$ - δ pyridine-d_5 = -0.17) observed for this methyl group in the ^1H nmr spectra of 22.

The application of this methodology to the total synthesis of sterpuric acid is currently under investigation in this laboratory.



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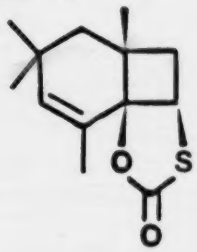
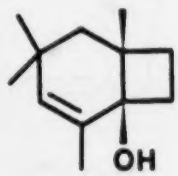


154



22

III. EXPERIMENTAL

General

Unless otherwise stated the following particulars apply. All reactions were run under a positive pressure of dry nitrogen. The nitrogen was purified by passage through a column (3.5 x 52 cm) of R-311 catalyst[89] and then through a similar column of Drierite and sodium hydroxide pellets. Reactions requiring anhydrous conditions were performed in oven dried glassware (115°C, 2h), cooled in a dessicator, quickly assembled, and sealed with rubber septa (when applicable) and purged with nitrogen. Anhydrous solvents were dried with suitable drying agents and distilled under nitrogen and were transferred by an oven dried syringe. During product isolation, solutions were dried with either anhydrous magnesium sulphate ($MgSO_4$) or anhydrous sodium sulphate (Na_2SO_4) and evaporated under water aspirator vacuum at 30°C and for non volatile compounds followed by evacuation of the flasks at 0.1 torr. The term *in vacuo* refers to solvent removal *via* Buchi rotoevaporator at water aspirator pressure. Solvents were distilled before use for chromatography or extraction. Anhydrous solvents were purified as follows: diethyl ether (Et_2O) and benzene (ArH) by distillation from a blue or purple solution of sodium benzophenone ketyl; tetrahydrofuran (THF) by

distillation from a blue or purple solution of potassium benzophenone ketyl; dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), 1,2-dichloroethane, pyridine, triethylamine (Et_3N), diisopropylamine, hexamethyldisilizane (HMDS), oxalyl chloride, ethanedithiol, acetonitrile, isophorone (J.T. Baker Chemical Co.), dimethylsulfoxide (DMSO) and hexamethylphosphoric triamide (HMPA) by distillation from calcium hydride (the latter two under reduced pressure and stored over molecular sieves (3Å) under nitrogen); methanol and ethanol by distillation over magnesium metal; acetone by distillation over $CaSO_4$; Skellysolve B refers to Skelly Oil Company light petroleum, b.p. 62-70°C; trichloroacetyl chloride (Aldrich) was initially distilled from calcium hydride and phosphorous oxychloride from potassium carbonate and both were freshly distilled when used. The commercial solutions (Aldrich) of methyl lithium in ether, n-butyllithium in hexane, and vinyllithium (Lochat) in THF were titrated before use by the diphenylacetic acid method.[90] Chlorophenoxythioformate,[49] tributyltin hydride,[50] and 1,1'-thiocarbonyldiimidazole[21] were prepared as reported in the literature. Vinyl chloroformate (PCR), catecholborane (Aldrich), diphenyldiselenide (Terochem), methyl-

triphenylphosphonium bromide (Aldrich), and pyridinium chlorochromate (Aldrich) were used as received.

Crystalline samples were recrystallized and liquid samples were subjected to Kugelrohr distillation before submitted for elemental analysis. Samples were routinely dried at 40-60°C/1 torr prior to analysis. Boiling points quoted for products distilled in a Kugelrohr apparatus refer to the oven temperature.

Flash column chromatography was performed by using E. Merck silica gel 60 (230-400 ASTM mesh) according to the procedure of Still.[91] Analytical thin layer chromatography (tlc) was carried out on aluminum sheets precoated (0.2 mm layer thickness) with silica gel $60F_{254}$ (E. Merck, Darmstadt). Preparative thin layer chromatography (ptlc) was carried out on glass plates (20 x 20 cm, 0.25 mm layer thickness) with the same absorbent (E. Merck, Darmstadt). Ultraviolet active materials were detected by visualization under a uv lamp (254 or 350 nm). For tlc, (only a thin vertical band in the case of ptlc) the visualization of the chromatograms was completed by spraying with a solution of phosphomolybdic acid (3%, w/v) containing ceric sulfate (0.5%, w/v) in sulfuric acid (3%, v/v), followed by careful charring on a hot plate.

Melting points were recorded on a Fisher-Johns melting point apparatus and are uncorrected. Fourier

transform infrared (ftir) spectra were recorded on a Nicolet 7199 FT interferometer. Single scan infrared (ir) spectra were recorded on a Perkim-Elmer 297 spectrophotometer. Ultraviolet (uv) spectra were recorded on a Hewlett-Packard HP8450A Diode Array spectrometer coupled to a 7470A plotter.

Proton nuclear magnetic resonance (^{1}H nmr) spectra were recorded on Bruker WP-80 (at 80 MHz), Bruker WH-200 (at 200 MHz), or a Bruker WH-400 (at 400 MHz) spectrometers in the specified deuterated solvent with tetramethylsilane (TMS) as an internal standard and measurements are reported in ppm downfield from TMS (δ). ^{13}C nuclear magnetic resonance (^{13}C nmr) spectra were measured on a Bruker HFX-90 (at 22.6 MHz), Bruker WH-200 (at 50.3 MHz) or Bruker WH-400 (at 100.6 MHz) spectrometers. For ^{13}C nmr, except where otherwise stated, deuterochloroform ($CDCl_3$) was employed as the internal standard (assigned as 77.06 ppm downfield from TMS) and measurements are reported in ppm downfield from TMS (δ).

Carbon-13 multiplicities were derived from gated decoupling spin echo experiments (GASPE).[65] Nuclear Overhauser enhancements (nOe) were determined by making all the data points of the control (undecoupled) spectrum negative and computer-adding it to the FID (free induction

decay) of the decoupled spectrum before Fourier transformation. Positive enhancements are defined as multiplets possessing an antiphase with respect to the decoupled signal. Samples for nOe measurements were deoxygenated with nitrogen for 10-15 min. prior to use. The following abbreviations are used in the text: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; J, coupling constant; and δ, chemical shift.

High resolution electron impact mass spectra (hreims) were recorded on an A.E.I. MS-50 mass spectrometer coupled to a DS 50 computer. Chemical ionization* mass spectra (cims) were obtained using an A.E.I. MS-9 mass spectrometer. The data is reported as m/z (relative intensity). Unless diagnostically significant, peaks with intensities less than 30% of the base peak are omitted. Combustion elemental analyses were performed by the microanalytical laboratory of the University of Alberta.

2-Acetoxy-3,5,5-trimethylcyclohex-2-enone 28

A solution of 31 (488.9 mg, 3.17 mmol, prepared according to a literature procedure[13]), pyridine (3 mL, 37.2 mmol), and acetic anhydride (0.60 mL, 6.30 mmol) in dry CH_2Cl_2 (25 mL) was stirred at room temperature for 20

*Ammonia as reagent gas

h. Aqueous HCl (5%, 40 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL), the organic layers were combined, washed with satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 28 (546.8 mg, 88%) as a yellowish white solid. m.p.: 52-54°C; tlc: R_f 0.28 (1:3 ethyl acetate/Skellysolve B); uv(methanol) λ max: 240 (ε 7710) nm; ftir ($CHCl_3$, cast): 1756, 1682, 1655 cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$) δ: 2.35 (s, 4H, 2 x CH_2), 2.23 (s, 3H, CH_3CO_2), 1.83 (s, 3H, $CH_3C{=}C$), 1.09 (s, 6H, 2 x CH_3); hreims: m/z calcd. for $C_{11}H_{16}O_3$ (M^+): 196.1099; found: 196.1097 (15), 154 (100), 98 (34).

(1SR,6RS)-7,7-Dichloro-6-methylbicyclo[4.2.0]octan-8-one (35)

This was prepared as previously described.[18] A 50-mL three-necked flask equipped with a condensor, addition funnel, magnetic stirrer, and nitrogen inlet was flame dried while purged with nitrogen. When cool, the flask was charged with 1-methylcyclohexene (1.14 g, 9.64 mmol), activated zinc (1.0 g, 15.5 mmol), and dry Et_2O (20 mL). The suspension was stirred at room temperature and a solution of dry trichloroacetyl chloride (1.1 mL, 10.0 mmol) and dry phosphorous oxychloride (0.92 mL, 10.0 mmol) in dry Et_2O (10 mL) was added dropwise by means of a syringe over a 1 h period. When addition of the solution

was completed, the mixture was heated under reflux with stirring for 2 h. The reaction mixture was then filtered through a pad of Celite and the unreacted zinc washed with Et_2O (25 mL). The combined organic extracts were concentrated *in vacuo* to *ca*. 25% of its original volume, an equal volume of *n*-pentane added, and the solution stirred for a few minutes to precipitate the zinc salts. The solution was decanted from the residue, washed successively with cold H_2O, cold satd $NaHCO_3$, satd NaCl, and dried (Na_2SO_4). The solvent was removed *in vacuo* and the residue was distilled bulb to bulb to afford **35** (1.06 g, 54%) as a colorless liquid. The spectra of **35** was identical with that reported in the literature.[18]

(1SR,6RS)-1-Acetoxy-7-chloro-6-methylbicyclo[4.2.0]octan-8-one **37**

A solution of dichloroketone **35** (3.60 g, 17.7 mmol) in dry acetone (40 mL) was treated with a mixture of glacial acetic acid (1.0 mL, 17.7 mmol) and triethylamine (2.5 mL, 17.9 mmol) in acetone (10 mL). The solution was stirred for 5 h at room temperature, then filtered to remove the triethylammonium chloride. In most cases, the acetone solution containing the crude product was used directly in the next reaction.

In one case, the acetone solution was concentrated to give the stereoisomeric chloroacetates 37 in 87% yield. tlc: R_f 0.45 (1:3 ethyl acetate/Skellysolve B); ir (film): 1770, 1720 cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$)δ : 5.15 (s, 3/5H, CHCl), 5.13 (s, 2/5H, CHCl), 2.10 (s, 3H, CH_3CO_2), 1.20-2.20 (m, 8H), 1.35 (s, 3H, CH_3). The singlets at δ 5.15 and δ 5.13 are present in the ratio of 3:2, indicative of the ratio of the two chloro stereoisomers present.

Chromous Chloride

A mixture of zinc dust (11.0 g, 168.3 mmol), mercuric chloride (0.77 g, 2.86 mmol), water (11 mL) and concentrated hydrochloric acid (0.57 mL) was stirred for 5 min and the liquid was decanted. Water (22 mL) and concentrated hydrochloric acid (2.0 mL) were added to the residue. The system was thoroughly purged with carbon dioxide and chromium (III) chloride hexahydrate (9.3 g, 35.4 mmol) was added. The resulting blue solution was transferred directly through a cannula to an acetone solution of chloroketone 37.

(1SR,6RS)-1-Acetoxy-6-methylbicyclo[4.2.0]octan-8-one 38

Freshly prepared chromous chloride solution (35.4 mmol) was transferred directly through a cannula to the

acetone solution of chloroketone 37 (prepared as described before and purged with carbon dioxide). The resultant solution was stirred for 5 h, then diluted with Et_2O and washed with water (2 x 100 mL), satd $NaHCO_3$ (75 mL), and satd NaCL (75 mL). The aqueous extracts were washed twice with ether and the combined ether extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Spectroscopic analysis (tlc, ir, ^1H nmr, *vide infra*) of the crude reaction mixture indicated the presence of some hydrolysis product, *cis*-ketoalcohol 39a (*ca*. 14%). The crude reaction mixture was dissolved in CH_2Cl_2 (5 mL) and treated with triethylamine (4.98 ml, 35.4 mmol), acetic anhydride (1.67 mL, 17.7 mmol) and 4-N,N-dimethylaminopyridine (1 crystal). After stirring at room temperature for 10 h, the reaction mixture was washed with 10% HCl followed by satd $NaHCO_3$. The aqueous layers were reextracted with CH_2Cl_2 (2 x 15 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated to a colorless oil. Bulb to bulb distillation of this oil at reduced pressure provided ketoacetate 38 (2.54 g, 82% from 35) as a colorless oil. b.p.: 80°C/0.5 torr; tlc: R_f 0.44 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1790, 1712 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$)δ : 3.08 (d, 1H, J=17 Hz, $CH_2C=O$), 2.52 (d, 1H, J=17 Hz, $CH_2C=O$), 2.08 (s, 3H, CH_3CO_2), 2.03 (m, 1H), 1.91-1.45 (m, 7H),

1.19 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 203.0 (s), 169.4 (s), 90.7 (s), 51.5 (t), 35.7 (s), 31.6 (t), 27.6 (t), 23.2 (q), 20.8 (q), 20.0 (t), 19.97 (t); hreims: m/z calcd. for $C_{11}H_{16}O_3$ (M^+): 196.1100; found: 196.1102 (0.2), 154 (24), 112 (100).

In another experiment the chromous chloride reduction was allowed to proceed for 64 h at room temperature. After workup ketoalcohols 39a+b was isolated in 50% yield as a colorless liquid. ^1H and ^{13}C nmr analysis indicate two stereoisomers are present in a ratio of 4:1. tlc: R_f 0.24, 0.23 (1:3 ethyl acetate/Skellysolve B); ir (film): 3450, 1775 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 3.90 (s, 1H, OH), 3.65 (s, 1H, OH), 3.08 (d, 1H, J=15.5 Hz, $CH_2C=O$), 2.42 (d, 1H, J=11.5 Hz, $CH_2C=O$), 2.18 (d, 1H, J=15.5 Hz, $CH_2C=O$), 1.98 (d, 1H, J=11.5 Hz, $CH_2C=O$), 1.91 - 1.37 (m, 8H), 1.23 (s, 3H, CH_3), 1.14 (s, 3H, CH_3). The two methyl singlets were present in the ratio of 4:1 indicative of the ratio of the two stereoisomers present.

The mixture of hydroxy acetates 39a+b was acetylated (Et_3N, Ac_2O, CH_2Cl_2, 4-DMAP) and after aqueous workup a mixture of ketoacetates 38 and 40 was obtained in 97% yield. ^1H nmr analysis of the acetoxyl methyl groups indicates that the isomers are present in a ratio of 4:1. A portion of this mixture was separated on ptlc (3 x 1:9 ethyl acetate/Skellysolve B). The major isomer had

spectral properties identical with those of 38 (vide supra). The minor isomer 40 displays the following properties. tlc: R_f 0.46 (1:3 ethyl acetate/Skellysolve B); ftir (film): 1790, 1740 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ : 2.42 (d, 1H, J=11.5 Hz, $CH_2C=O$), 2.27 (d, 1H, J=11.5 Hz, $CH_2C=O$), 2.07 (s, 3H, CH_3CO_2), 1.90 (m, 1H), 1.77 (m, 3H), 1.54 (m, 4H), 1.35 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 211.1 (s), 169.4 (s), 89.9 (s), 55.8 (t), 35.4 (s), 33.9 (t), 30.2 (t), 24.1 (t), 22.9 (q), 22.7 (t), 20.8 (q); hreims: m/z calcd. for $C_{11}H_{16}O_3$ (M^+): 196.1099; found: 196.1090 (5), 154 (42), 136 (32), 126 (88), 111 (66), 108 (39), 97 (56), 55 (100).

(1SR,6RS,8RS)-1-Hydroxy-6-methylbicyclo[4.2.0]octan-8-ol 41 and (1SR,6RS,8SR)-1-Hydroxy-6-methylbicyclo[4.2.0]-octan-8-ol 42

A mixture of ketoacetate 38 (311.5 mg, 1.59 mmol) and lithium aluminum hydride (72.2 mg, 1.90 mmol) in Et_2O (10 mL) was refluxed for 3 h. Ethanol was added slowly to destroy the excess lithium aluminum hydride. The mixture was poured into Et_2O (10 mL) and washed with 10% HCl (10 mL), satd $NaHCO_3$ (10 mL), and satd NaCl (10 mL). The aqueous washings were extracted with Et_2O (2 x 20 mL) and the combined ether extracts were dried ($MgSO_4$), filtered, and concentrated. Separation of the residue by flash

chromatography (1:1 ethyl acetate/Skellysolve B) afforded 41 (81.7 mg, 33%) and 42 (69.3 mg, 28%). Analytical samples of 41 and 42 were obtained by recrystallization. Compound 41 was recrystallized from n-pentane and has the following properties: m.p.: 73-74°C; tlc: R_f 0.09 (1:3 ethyl acetate/Skellysolve B); ftir (CCl_4): 3400 cm^{-1}; ftir (CCl_4, diluted): 3400 cm^{-1} peak; ^1H nmr (400 MHz, $CDCl_3$) δ: 4.12 (t, 1H, J=7 Hz, $CH_2\underline{CH}O$), 2.30 (m, 2H, 2 x OH), 1.96 (dd, 1H, J=7, 11 Hz, $\underline{CH_2}CHO$), 1.67 (m, 3H), 1.63 (dd, 1H, J=7, 11 Hz, $\underline{CH_2}CHO$), 1.33 (m, 5H), 1.02 (s, 3H, CH_3); ^1H nmr (400 MHz, pyridine-$\underline{d}_5$) δ: 6.20, 5.60 (2 brs, 2H, 2 x OH), 4.48 (t, 1H, J=7.5 Hz, $CH_2\underline{CH}O$), 2.07 (dd, 1H, J=7.5, 10.5 Hz, $\underline{CH_2}CHO$), 2.02 (dd, 1H, J=7.5, 10.5 Hz, $\underline{CH_2}CHO$), 1.93 (m, 1H), 1.59 (m, 3H), 1.34 (m, 3H), 1.23 (s, 3H, CH_3), 1.18 (m, 1H); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 77.9 (s), 66.9 (d), 42.0 (t), 38.3 (t), 36.3 (s), 32.5 (t), 23.3 (t), 21.9 (t), 20.0 (q); hreims: m/z calcd. for $C_9H_{16}O_2$ (M^+): 156.1150; found: 156.1144 (3), 112 (100), 97 (44), 82 (33); Analysis: calcd. for $C_9H_{16}O_2$: C 69.19, H 10.32; found: C 68.90, H 10.15.

Compound 42 was recrystallized from dichloromethane/Skellysolve B and has the following properties: m.p.: 121-123°C; tlc: R_f 0.02 (1:3 ethyl acetate/Skellysolve B); ftir (CCl_4): 3600, 3282 cm^{-1}; ftir (CCl_4, diluted): 3600 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$)δ: 4.11 (t,

1H, J=8.5 Hz, $CH_2\underline{CH}O$), 2.08 (brs, 2H, 2 x OH), 1.88 (m, 1H), 1.69 (dd, 1H, J=8.5, 11 Hz, $\underline{CH_2}CHO$), 1.59 (m, 3H), 1.52 (dd, 1H, J=8.5, 11 Hz, $\underline{CH_2}CHO$), 1.45 (m, 1H), 1.22 (m, 3H), 1.08 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, CD_2Cl_2) δ: 77.1 (s), 74.3 (d), 35.6 (s), 33.9 (t), 33.6 (t), 29.7 (t), 24.5 (q), 22.8 (t), 20.8 (t); hreims: m/z calcd. for $C_9H_{16}O_2$ (M^+): 156.1150; found: 156.1151 (1), 112 (100), 97 (41); Analysis: calcd. for $C_9H_{16}O_2$: C 69.19, H 10.32; found: C 69.34, H 10.32.

(1SR,6RS,8RS)-6-Methyl-9,11-dioxatricyclo[6.3.0.$0^{1,6}$]-undec-10-thione 43

A mixture of cis-diol 41 (82.3 mg, 0.53 mmol) and 1,1'-thiocarbonyldiimidazole (244.8 mg, 1.37 mmol) in 1,2-dichloroethane (3 mL) was heated under reflux for 11 h. Most of the solvent was removed in vacuo and the residue was subjected to flash chromatography (1:3 ethyl acetate/Skellysolve B) to give 43 as a yellowish white solid. An analytical sample of 43 was prepared by recrystallizaton from Skellysolve B. m.p.: 74-75°C; tlc: R_f 0.31 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1460 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.06 (dd, 1H, J=5, 7.5 Hz, $CH_2\underline{CH}O$), 2.29 (dd, 1H, J=7.5, 13 Hz, $\underline{CH_2}CHO$), 2.08 (dd, 1H, J=5, 13 Hz, $\underline{CH_2}CHO$), 1.93 (m, 3H), 1.74 (m, 1H), 1.59 (m, 1H), 1.35 (m, 3H), 1.19 (s, 3H,

CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 192.7 (s), 98.2 (s), 78.6 (d), 41.6 (t), 39.8 (s), 39.2 (t), 27.3 (t), 22.6 (t), 20.3 (t), 19.4 (q); hreims: m/z calcd. for $C_{10}H_{14}O_2S$ (M^+): 198.0714; found: 198.0714 (100), 109 (71), 95 (31), 94 (47), 81 (36), 79 (51), 67 (75), 55 (40); Analysis: calcd. for $C_{10}H_{14}O_2S$: C 60.57, H 7.12, S 16.17; found: C 60.43, H 7.04, S 15.96.

(1SR,6RS,8SR)-8-[(Imidazole-N-thiocarbonyl)oxy]-6-methylbicyclo[4.2.0]octan-1-ol 44

A mixture of trans-diol 42 (19.7 mg, 0.13 mmol) and 1,1'-thiocarbonyldiimidazole (90.0 mg, 0.51 mmol) in 1,2-dichloroethane (3 mL) was heated under reflux for 16 h. Most of the solvent was removed in vacuo. Purification of the residue by flash chromatography (1:1 ethyl acetate/Skellysolve B) gave 44 as a white solid. An analytical sample was prepared by recrystallization from Skellysolve B. m.p.: 89-90°C; tlc: R_f 0.34 (3:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3300, 1530, 1460 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 8.33 (brs, 1H), 7.61 (brs, 1H), 7.05 (brs, 1H), 5.41 (t, 1H, J=8 Hz, $CH_2\underline{CH}O$), 2.94 (brs, 1H, OH), 2.02 (dd, 1H, J=8, 10.5 Hz, $\underline{CH_2}CHO$), 1.88 (dd, 1H, J=8, 10.5 Hz, $\underline{CH_2}CHO$), 1.68 (m, 5H), 1.32 (m, 3H), 1.22 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 184.1 (s), 136.8 (d), 130.9 (d), 118.0 (d),

83.9 (d), 76.2 (s), 35.7 (s), 32.9 (t), 31.2 (t), 31.1 (t), 24.5 (q), 22.0 (t), 19.8 (t); hreims: m/z calcd. for $C_6H_7N_2OS$ ($M^+-C_7H_{11}O$, parent ion not seen); 155.0279; found: 155.0276 (92), 139 (76), 112 (79), 97 (47), 94 (33), 79 (35), 69 (100), 68 (54), 67 (36), 55 (47); Analysis: calcd. for $C_{10}H_{14}O_2S$: C 60.57, H 7.12, S 16.17; found: C 60.43, H 7.04, S 15.96.

3,5,5-Trimethylcyclohex-2-en-1-ol 51

Sodium borohydride (16.1 g, 0.42 mol) was added in small portions over 0.5 h to a stirred solution of isophorone (50.0 g, 0.36 mol) in MeOH (450 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred at room temperature for 2 h, then acetic acid (10 mL) was added. Most of the methanol was removed *in vacuo* and the residue was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic extracts were washed with 10% HCl (100 mL), satd $NaHCO_3$ (100 mL), dried (Na_2SO_4), filtered, and concentrated to a yellow liquid. Evaporative distillation at reduced pressure afforded 51 (36.0 g, 71%) as a colorless oil. b.p.: 75°C/0.5 torr; tlc: R_f 0.33 (1:1 ethyl acetate/Skellysolve B); ir (film): 3350, 1675 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.36 (brs, 1H, C=CH), 4.17 (brs, 1H, $W_{\frac{1}{2}}$=20 Hz, $CH_2\underline{CH}O$), 1.86 (brs, 1H, $W_{\frac{1}{2}}$=8 Hz, OH), 1.79 (brd, 1H, J=17 Hz, CH_2), 1.70 (brdd, J=6, 12.5

Hz, $\underline{CH_2}CHO$), 1.62 (brs, 3H, $CH_3C{=}C$), 1.55 (brd, 1H, J=17 Hz, CH_2), 1.18 (dd, 1H, J=9.5, 12.5 Hz, $\underline{CH_2}CHO$), 0.94 (s, 3H, CH_3), 0.83 (s, 3H, CH_3); hreims: m/z calcd. for $C_9H_{16}O$ (M^+): 140.1202; found: 140.1203 (27), 125 (100), 107 (41), 84 (55).

1-Methoxy-3,5,5-trimethylcyclohex-2-ene 49

Sodium hydride (2.48 g of a 60% dispersion in oil, 0.062 mmol) was rinsed three times with Skellysolve B under a nitrogen atmosphere. THF (100 mL) was added and the suspension was cooled to 0°C in an ice-water bath. A solution of alcohol 51 (5.2 g, 37.1 mmol) in THF (10 mL) was added in portions. After stirring for 1 h, neat methyl iodide (4.44 mL, 71.3 mmol) was added in one portion and the reaction mixture was heated under reflux for 4 h. Satd NH_4Cl (5 mL) was added. The solvent was removed in vacuo and the residue was partitioned between CH_2Cl_2 and H_2O. The aqueous extracts were reextracted with CH_2Cl_2 (2 x 50 mL) and the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated to give a light yellow liquid. Evaporative distillation at reduced pressure afforded 49 (5.77 g, 102%) as a colorless liquid: b.p.: 85°C/water aspirator vacuum; tlc: R_f 0.21 (1:19 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1672 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 5.45 (m, 1H, $W_{\frac{1}{2}}$=5Hz,

C=CH), 3.77 (m, 1H, $W_{\frac{1}{2}}$=17 Hz, $CH_2\underline{CH}O$), 3.22 (s, 3H, CH_3O), 1.84 (brd, 1H, J=17.5 Hz, CH_2), 1.69 (hidden ddt, 1H, J=6, 12.5, 1.5 Hz, $\underline{CH_2}CHO$), 1.64 (brs, 3H, CH_3C=C), 1.57 (brd, 1H, J=17.5 Hz, CH_2), 1.22 (dd, 1H, J=9, 12.5 Hz, $\underline{CH_2}CHO$), 0.95 (s, 3H, CH_3), 0.85 (s, 3H, CH_3); ^{13}C nmr (50.3 MHz, $CDCl_3$)δ : 136.4 (s), 120.9 (d), 75.5 (d), 55.5 (q), 44.4 (t), 41.0 (t), 31.2 (q), 30.8 (s), 26.5 (q), 23.6 (q); hreims: m/z calcd. for $C_{10}H_{18}O$ (M^+): 154.1391; found: 154.1352 (24), 139 (100), 107 (64), 98 (30), 91 (33).

1-Hydroxy-1,3,5,5-tetramethylcyclohex-2-ene 52

A solution of isophorone (922.9 mg, 6.68 mmol) in Et_2O (50 mL) was cooled to 0°C in an ice-water bath and methyllithium (8.0 mL, 8.00 mmol, 1.0 M in diethyl ether) was added. The reaction mixture was stirred for 3 h at room temperature then satd NH_4Cl (5 mL) was added. The ether extracts were washed with satd $NaHCO_3$ (25 mL), H_2O (25 mL), and satd NaCl (25 mL), dried ($MgSO_4$), filtered, and concentrated to a light yellow oil. Evaporative distillation at reduced pressure gave 52 (796.8 mg, 77%) as a colorless oil. b.p.: 70°C/1.2 torr; tlc: R_f 0.31 (1:3 ethyl acetate/Skellysolve B); ^1H nmr (80 MHz, $CDCl_3$)δ : 5.40 (brs, 1H, C=CH), 1.77 (s, 2H, CH_2), 1.70 (s, 1H, OH), 1.70 (s, 3H, CH_3C=C), 1.70 (d, 1H, J=14 Hz,

CH_2), 1.55 (d, 1H, J=14 Hz, CH_2), 1.30 (s, 3H, CH_3CO), 1.08 (s, 3H, CH_3), 0.99 (s, 3H, CH_3).

1-Methoxy-1,3,5,5-tetramethylcyclohex-2-ene 50

Potassium hydride (1.87 g of a 24% dispersion in oil, 11.2 mmol) was rinsed three times with Skellysolve B under a nitrogen atmosphere. DMF (25 mL) was added and the suspension was cooled in an ice-water bath. A solution of alcohol 52 (564.5 mg, 3.66 mmol) in DMF (4 mL) was added in portions. After stirring for 1 h, methyl iodide (0.34 mL, 5.49 mmol) was added in one portion and the reaction mixture was stirred at room temperature for 3 h. Water (20 mL) was added and the product was extracted with Et_2O (2 x 55 mL). The combined organic extracts were washed with H_2O, satd NaCl, dried ($MgSO_4$), filtered, and concentrated to a pale yellow oil. Evaporative distillation at reduced pressure afforded 50 (543.1 mg, 88%) as a colorless oil. b.p.: 120°C/water aspirator vacuum; tlc: R_f 0.56 (1:3 ethyl acetate/Skellysolve B); ir (film): 1670 cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$) δ : 5.33 (brs, 1H, C=CH), 3.15 (s, 3H, CH_3O), 1.70 (s, 2H, CH_2), 1.70 (s, 3H, $CH_3C=C$), 1.65 (d, 1H, J=14 Hz, CH_2), 1.51 (d, 1H, J=14 Hz, CH_2), 1.20 (s, 3H, CH_3CO), 0.98 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); hreims: m/z calcd. for $C_{11}H_{20}O$ (M^+): 168.1514; found: 168.1512 (4), 153 (100), 121 (53).

3,5,5-Trimethyl-2-[(2-oxabut-3-enoyl)oxy]cyclohex-2-enone 24

Vinyl chloroformate (6.80 mL, 74.0 mmol) was added to a solution of 31 (9.25 g, 60.0 mmol) and pyridine (10.0 mL, 0.124 mol) in dry CH_2Cl_2 (100 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred for 15 h at room temperature then washed with 5% HCl (100 mL) and satd $NaHCO_3$ (100 mL). The aqueous layers were washed with CH_2Cl_2 (2 x 100 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated under reduced pressure to afford 24 (13.62 g, 100%) as a light yellow oil which was sufficiently pure to be used in the next step. A portion of this material was subjected to bulb to bulb distillation to afford 24 as a colorless oil. b.p.: 110°C/0.7 torr; tlc: R_f 0.35 (1:9 diethyl ether/petroleum ether b.p. 30-60°C); ir (CCl_4): 3100, 1770, 1690, 1645 cm^{-1}; uv (methanol) λ max: 238 (ε 8442) nm, 310 (ε 48) nm; ^1H nmr (100 MHz, $CDCl_3$) δ: 7.07 (dd, 1H, J=6, 13 Hz, $\underline{CH}=CH_2$), 4.98 (dd, 1H, J=2, 13 Hz, $CH=\underline{CH_2}$), 4.63 (dd, 1H, J=2, 6 Hz, $CH=\underline{CH_2}$), 2.38 (s, 4H, 2 x CH_2), 1.91 (s, 3H, $CH_3C=C$), 1.10 (s, 6H, 2 x CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 190.0 (s), 150.0 (s), 144.8 (s), 142.4 (d), 140.7 (s), 98.1 (t), 50.6 (t), 44.8 (t), 32.9 (s), 22.7 (2q), 17.3 (q); hreims: m/z calcd. for $C_{12}H_{16}O_4$ (M^+):

224.1048; found: 224.1048 (1), 181 (100), 137 (32), 81 (39); Analysis: calcd. for $C_{12}H_{16}O_4$: C 64.27, H 7.19; found: C 64.31, H 7.12.

(1RS,6RS,8RS)-1,8-Carbonyldioxy-4,4,6-trimethylbicyclo-[4.2.0]octan-2-one 25

A degassed solution of 24 (4.473 g, 19.95 mmol) in dry acetone (500 mL) was irradiated with a 450-W medium pressure mercury lamp in a quartz immersion well through a Pyrex filter for 34 h (see also Table 1). The solvent was removed in vacuo. The residue was purified by flash chromatography eluting with 1:2 ethyl acetate/Skellysolve B to give unreacted 24 (2.124 g, 47%) and 25 (1.908 g, 43%, 81% based on starting material consumed) as a white solid (m.p. 133-136°C). This material was pure enough to be used in subsequent steps. A portion was recrystallized from diethyl ether/Skellysolve B to afford 25 as colorless prisms. m.p.: 148-149°C; tlc: R_f 0.09 (1:3 ethyl acetate/Skellysolve B); ir ($CHCl_3$): 1810, 1725 cm^{-1}; uv (methanol) λ max: 239 (ε 368) nm; ^1H nmr (100 MHz, $CDCl_3$) δ: 4.99 (dd, 1H, J=5, 6 Hz, $CH_2\underline{CH}O$), 2.51 (dd, 1H, J=6, 14 Hz, $\underline{CH_2}CHO$), 2.41 (brs, 2H, $CH_2C{=}O$), 2.15 (dd, 1H, J=5, 14 Hz, $\underline{CH_2}CHO$), 1.92 (brs, 2H, CH_2), 1.34 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 0.98 (s, 3H, CH_3); ^{13}C nmr (22.6 MHz, $CDCl_3$) δ: 201.4 (s), 155.2 (s), 87.6 (s),

73.9 (d), 52.7 (t), 50.9 (t), 44.7 (t), 43.0 (s), 35.2 (s), 31.3 (q), 26.5 (q), 23.6 (q); hreims: m/z calcd. for $C_{12}H_{16}O_4$ (M^+): 224.1049; found: 224.1046 (39), 209 (13), 96 (100), 83 (35), 55 (39); Analysis: calcd. for $C_{12}H_{16}O_4$: C 64.27, H 7.19; found: C 63.97, H 7.12.

(1RS,6RS,8RS)-1,8-Carbonyldioxy-4,4,6-trimethyl-2-methylenebicyclo[4.2.0]octane 62

n-Butylithium (1.51 mL, 2.58 mmol, 1.71 M solution in hexane) was added to a stirred suspension of methyltriphenylphosphonium bromide (1.014 g, 2.84 mmol) in dry THF (35 mL) cooled to 0°C in an ice-water bath. The resulting solution was stirred for 15 min then cooled to -78°C in a dry ice-acetone bath. A solution of ketone 25 (578.0 mg, 2.58 mmol) in dry THF (10 mL) was added via syringe and the resulting solution was allowed to warm to room temperature and stirred for 2 h. Water (10 mL) was added, THF was removed in vacuo, and the resulting reaction mixture was extracted with CH_2Cl_2 (3 x 100 mL). The organic extracts were combined, dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash column chromatography of the residue eluting with 1:9 ethyl acetate/Skellysolve B gave in order of elution 62 (507.6 mg, 89%) as colorless crystals and 61 (11.4 mg, 2%, vide infra) as a white solid. A portion of 62 was

recrystallized (petroleum ether b.p. 30-60°C) to afford 62 as colorless needles: m.p.: 82-83°C; tlc: R_f 0.72 (1:3 ethyl acetate/Skellysolve B); ir ($CHCl_3$): 1800, 1645 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ : 5.20 (brs, 1H, C=CH_2), 4.93 (d, 1H, J=1 Hz, C=CH_2), 4.85 (dd, 1H, J=5, 6 Hz, CH_2CHO), 2.30 (dd, 1H, J=6, 14 Hz, CH_2CHO), 2.15 (brs, 2H, CH_2), 1.95 (dd, 1H, J=5, 14 Hz, CH_2CHO), 1.81 (dd, 1H, J=1, 14 Hz, CH_2), 1.54 (d, 1H, J=14 Hz, CH_2) 1.22 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C nmr (22.6 MHz, $CDCl_3$) δ: 156.0 (s), 139.6 (s), 112.1 (t), 90.1 (s), 75.0 (d), 52.1 (t), 46.5 (t), 44.5 (t), 41.0 (s), 32.3 (s), 31.9 (q), 25.4 (q), 22.8 (q); hreims: m/z calcd. for $C_{13}H_{18}O_3$ (M^+): 222.1254; found: 222.1251 (40), 178 (22), 163 (91), 135 (52), 123 (30), 122 (48), 109 (34), 107 (48), 96 (40), 95 (46), 94 (35), 93 (59), 91 (33), 81 (65), 79 (75), 77 (36), 69 (40), 67 (77), 55 (100), 53 (46); Analysis: calcd. for $C_{13}H_{18}O_3$: C 70.24, H 8.16; found: C 70.28, H 8.39.

(1RS,6RS,8RS)-4,4,6-Trimethyl-2-methylenebicyclo[4.2.0]-octane-1,8-diol 61

A solution of carbonate 62 (507.6 mg, 2.29 mmol) and potassium carbonate (474 mg, 3.43 mmol) in 1:1 MeOH/H_2O (30 mL) was heated under reflux for 4 h. The reaction mixture was concentrated in vacuo and the aqueous residue was extracted with CH_2Cl_2 (3 x 40 mL). The organic

extracts were combined, dried (Na_2SO_4), and concentrated *in vacuo* to afford **61** (426.7 mg, 95%) as a white solid (m.p. 107-109°C). A portion of this was purified by recrystallization (diethyl ether/petroleum ether b.p. 30-60°C) to give **61** as colorless rods: m.p.: 111-112°C; tlc: R_f 0.09 (1:3 ethyl acetate/Skellysolve B); ftir (CCl_4): 3600, 3520, 1640 cm^{-1}; ftir (CCl_4-dilution): 3600, 3520, 1640 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ : 5.12 (t, 1H, J=1.5 Hz, C=CH_2), 4.84 (t, 1H, J=1.5 Hz, C=CH_2), 4.30 (brt, 1H, J=7.5 Hz, CH_2CHO), 2.51, 2.43 (2 brs, 2H, 2 x OH), 2.25 (d, 1H, J=14 Hz, CH_2C=C), 2.10 (dd, 1H, J=3, 14 Hz, CH_2C=C), 2.09 (dd, 1H, J=7.5, 10 Hz, CH_2CHO), 1.78 (dd, 1H, J=7.5, 10 Hz, CH_2CHO), 1.67 (dd, 1H, J=3, 14 Hz, CH_2), 1.55 (d, 1H, J=14 Hz, CH_2), 1.15 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^1H nmr (400 MHz, pyridine-d_5) δ : 6.79 (brd, 1H, OH), 5.58 (brs, 1H, C=CH_2), 5.00 (brs, 1H, OH), 4.93 (brs, 1H, C=CH_2), 4.60 (apparent q, 1H, J=7.5 Hz, CH_2CHO), 2.29 (brd, 1H, J=14 Hz, CH_2C=C), 2.17 (dd, 1H, J=7.5, 9.5 Hz, CH_2CHO), 2.12 (dd, 1H, J=7.5, 9.5 Hz, CH_2CHO), 2.05 (brd, 1H, J=14 Hz, CH_2C=C), 1.57 (d, 1H, J=14 Hz, CH_2), 1.53 (d, 1H, J=14 Hz, CH_2), 1.30 (s, 3H, CH_3), 0.89 (s, 6H, 2 x CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 147.1 (s), 109.0 (t), 79.5 (s), 66.7 (d), 51.7 (t), 47.1 (t), 45.1 (t), 37.7 (s), 32.4 (s), 32.3 (q), 26.0 (q), 22.9 (q); hreims: calcd. for

$C_{12}H_{20}O_2$ (M^+); 196.1463; found: 196.1458 (4), 152 (100), 137 (94), 109 (21); Analysis: calcd. for $C_{12}H_{20}O_2$: C 73.43, H 10.27; found: C 73.63, H 10.52.

2-[(2-Oxabut-3-enoyl)oxy]cyclohex-2-enone 63

Vinyl chloroformate (3.15 mL, 34.3 mmol) was added to a solution of freshly distilled cyclohexane-1,2-dione (3.34 g, 29.8 mmol) and pyridine (3.10 mL, 39.9 mmol) in dry CH_2Cl_2 (100 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred at room temperature for 31 h, then washed with 5% HCl (100 mL) and satd $NaHCO_3$ (100 mL). The aqueous layers were washed with CH_2Cl_2 (2 x 100 mL) and the organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Bulb to bulb distillation of the residue afforded 63 (4.95 g, 91%) initially as a colorless oil which crystallizes and discolors on standing. b.p.: 90°C/0.08 torr; m.p.: 32-34°C; ftir ($CHCl_3$, cast): 3100, 1775, 1690, 1650 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 7.08 (dd, 1H, J=6, 14 Hz, $\underline{CH}=CH_2$), 6.77 (t, 1H, J=4.5 Hz, $CH_2\underline{CH}=C$), 5.02 (dd, 1H, J=2, 13.5 Hz, $\underline{CH}=CH_2$), 4.68 (dd, 1H, J=2, 6 Hz, $CH=\underline{CH_2}$), 2.60 (m, 2H, $CH_2C=O$), 2.55 (apparent dt, 2H, J=4.5, 6.0 Hz, $\underline{CH_2}CH=C$), 2.11 (m, 2H, CH_2); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ: 191.1 (s), 150.5 (s), 145.0 (s), 142.6 (d), 136.1 (d), 98.8 (t), 38.0 (t), 24.7

(t), 22.5 (t); hreims: m/z calcd. for $C_7H_7O_3$ ($M^+-C_2H_3O$, parent ion not seen): 139.0395; found: 139.0394 (100), 95 (31), 67 (42); Analysis: calcd. for $C_9H_{10}O_4$: C 59.34, H 5.53; found: C 59.70, H 5.66.

5,5-Dimethyl-3-[(2-oxabut-3-enoyl)oxy]cyclohex-2-enone 64

Vinyl chloroformate (2.30 mL, 25.0 mmol) was added to a solution of 5,5-dimethyl-1,3-cyclohexanedione (2.91 g, 20.7 mmol) and pyridine (2.60 mL, 32.2 mmol) in dry CH_2Cl_2 (100 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred for 15 h at room temperature, then washed with 5% HCl (100 mL) and satd $NaHCO_3$. The aqueous layers were washed with CH_2Cl_2 (2 x 100 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Bulb to bulb distillation of the residue afforded 64 (4.02 g, 92%) as a colorless oil which discolors on standing. b.p.: 100°C/1 torr; tlc: R_f 0.19 (1:9 ethyl acetate/Skellysolve B); ftir (film): 3100, 1777, 1677, 1651 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 7.06 (dd, 1H, J=6, 13.5 Hz, $\underline{CH}=CH_2$), 6.07 (t, 1H, J=0.8 Hz, C=CH), 5.04 (dd, 1H, J=2.5, 13.5 Hz, $CH=\underline{CH_2}$), 4.72 (dd, 1H, J=2.5, 6.0 Hz, $CH=\underline{CH_2}$), 2.48 (d, 2H, J=0.8 Hz, CH_2), 2.29 (s, 2H, $CH_2C=O$), 1.12 (s, 6H, 2 x CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$)δ : 198.5 (s), 166.7 (s), 148.5 (s), 141.9 (d), 115.7 (d), 99.2 (t), 50.5 (t), 41.3

(t), 32.8 (s), 27.9 (2q); hreims: m/z calcd. for $C_{11}H_{14}O_4$ (M^+): 210.0892; found: 210.0890 (26), 123 (43), 84 (100), 67 (35); Analysis: calcd. for $C_{11}H_{14}O_4$: C 62.85, H 6.71; found: C 62.97, H 6.64.

2-Methyl-3-[(2-oxabut-3-enoyl)oxy]cyclohex-2-enone 65

Vinyl chloroformate (3.34 mL, 36.4 mmol) was added to a solution of 2-methyl-1,3-cyclohexanedione (3.83 g, 30.3 mmol) and pyridine (3.66 mL, 45.5 mmol) in dry CH_2Cl_2 (100 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred at room temperature for 7 h then washed with 5% HCl (100 mL) and satd $NaHCO_3$ (100 mL). The aqueous layers were washed with CH_2Cl_2 (2 x 100 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Bulb to bulb distillation of the residue afforded 65 (5.67 g, 95%) as a colorless oil. b.p.: 105°C/2.0 torr; tlc: R_f 0.52 (1:1 ethyl acetate/Skellysolve B); ir (film): 3100, 1770, 1680, 1650 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ : 7.10 (dd, 1H, J=6, 14 Hz, $\underline{CH}=CH_2$), 5.05 (dd, 1H, J=2, 14 Hz, $CH=\underline{CH_2}$), 4.72 (dd, 1H, J=2, 6 Hz, $CH=\underline{CH_2}$), 2.65 (m, 2H), 2.48 (m, 2H), 2.07 (m, 2H), 1.75 (t, 3H, J=2Hz, $CH_3C=C$); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 198.8 (s), 162.9 (s), 149.0 (s), 142.3 (d), 125.1 (s), 99.1 (t), 36.8 (t), 27.9 (t), 20.7 (t), 8 (q); hreims: m/z calcd. for $C_{10}H_{12}O_4$ (M^+):

196.0736; found: 196.0735 (54), 126 (48), 109 (32), 98 (100); Analysis: calcd. for $C_{10}H_{12}O_4$: C 61.22, H 6.16; found: C 61.47, H 6.38.

(1RS,6RS,8RS)-1,8-Carbonyldioxybicyclo[4.2.0]octan-2-one 66

A degassed solution of 63 (2.112 g, 11.59 mmol) in dry acetone (200 mL) was irradiated with a 250-W medium pressure mercury lamp through a Pyrex filter for 28 h. The solvent was removed in vacuo. The residue was purified by flash chromatography with 1:1 ethyl acetate/Skellysolve B to afford unreacted 63 (92.2 mg, 4%) and 66 (1.2933 g, 60%, light yellow solid, m.p. 59-62°C). Compound 66 was sufficiently pure to be used in the next reaction. A portion of 66 was recrystallized from diethyl ether/methanol to afford an analytical sample of 66 as white crystals. m.p.: 78-79°C; tlc: R_f 0.23 (1:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1801, 1719 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ : 5.00 (dd, 1H, J=4.5, 6.5 Hz, $CH_2\underline{CH}O$) 3.11 (tt, 1H, J=5.5, 10.5 Hz, $\underline{CH}CH_2$), 2.68 (ddd, 1H, J=4.5, 10.5, 14.5 Hz, $\underline{CH_2}CHO$), 2.64 (m, 1H), 2.51 (m, 1H), 2.40 (ddd, 1H, J=5.5, 6.5, 14.5 Hz, $\underline{CH_2}CHO$), 2.01 (m, 3H), 1.72 (m, 1H); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ : 202.0 (s), 154.9 (s), 84.6 (s), 75.5 (d), 39.1 (d), 39.0 (t), 32.8 (t), 28.1 (t), 19.0 (t); hreims: m/z calcd. for

$C_9H_{10}O_4$ (M^+): 182.0579; found: 182.0579 (39), 128 (38), 109 (32), 95 (31), 82 (45), 67 (59), 55 (100), 54 (60); Analysis: calcd. for $C_9H_{10}O_4$: C 59.34, H 5.53; found: C 59.31, H 5.46.

Irradiation of vinyl carbonate 64

A degassed solution of 64 (1.6 g, 7.61 mmol) in dry acetone (250 mL) was irradiated with a 450-W medium pressure Hanovia mercury lamp through a Pyrex filter for 20 h. The reaction was monitored by tlc and irradiation was discontinued after the disappearance of ca. 70% of 64. The solvent was removed in vacuo. The residue was purified by flash chromatography eluting with 2:5 ethyl acetate/Skellysolve B. The following compounds listed in order of elution were isolated: unreacted 64 (441 mg, 28%), 67 (168 mg, 20%), and 68 (119 mg, 10%). Compounds 67 and 68 were converted (pyridine, Ac_2O, CH_2Cl_2, 4-DMAP) to the monoacetate derivatives 69 and 70, respectively, for easier characterization. Analytically samples of 69 and 70 were obtained by bulb to bulb distillation.

3-(1-Acetoxyethyl)-5,5-dimethylcyclohex-2-enone 69

b.p.: 90°C/10 torr; tlc: R_f 0.25 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1743, 1672, 1635 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 6.01 (dd, 1H, J=1.5, 2.2 Hz, CH=C), 5.25 (q, 1H, J=6.5 Hz, $CH_3\underline{CH}O$), 2.25

(s, 2H, $CH_2C{=}O$), 2.22 (dd, 1H, J=1.5, 17.5 Hz, $CH_2C{=}C$), 2.15 (dd, 1H, J=2.2, 17.5 Hz, $\underline{CH_2}C{=}C$), 2.09 (s, 3H, CH_3CO_2), 1.37 (d, 3H, J=6.5 Hz $\underline{CH_3}CHO$), 1.05 (s, 3H, CH_3), 1.04 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$)δ : 199.7 (s), 169.8 (s), 161.1 (s), 122.9 (d), 71.6 (d), 51.2 (t), 40.1 (t), 28.0 (2q), 20.9 (q), 18.6 (q); hreims: m/z calcd. for $C_{12}H_{18}O_3$ (M^+): 210.1256; found: 210.1256 (25), 168 (100), 139 (54), 112 (42); Analysis: calcd. for $C_{12}H_{18}O_3$: C 68.55, H 8.63; found: C 68.64, H 8.56.

3-(1-Acetoxy-4-oxopentyl)-5,5-dimethylcyclohex-2-enone 70

b.p.: 106°C/0.7 torr; tlc: R_f 0.23 (1:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1745, 1717, 1671, 1630 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$)δ : 5.97 (brs, 1H, $\underline{CH}{=}C$), 5.04 (dd, 1H, J=4, 8 Hz, $CH_2\underline{CH}O$), 2.52 (t, 2H, J=7 Hz, $\underline{CH_2}CH_2$), 2.24 (s, 2H, CH_2), 2.22 (brs, 2H, CH_2), 2.16 (s, 3H, CH_3CO_2), 2.10 (s, 3H, $CH_3C{=}O$), 2.07 (m, 1H, $\underline{CH_2}CHO$), 1.88 (ddt, 1H, J=8, 14, 7 Hz, $\underline{CH_2}CHO$), 1.05 (s, 6H, 2 x CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$)δ : 206.7 (s), 199.3 (s), 169.8 (s), 159.7 (s), 123.5 (d), 74.3 (d), 51.2 (t), 40.2 (t), 38.6 (t), 33.6 (s), 29.9 (q), 28.0 (2q), 26.1 (t), 20.7 (q); hreims: calcd. for $C_{15}H_{22}O_4$ (M^+): 266.1518; found: 266.1518 (22), 224 (100), 206 (51), 163 (36), 149 (30), 148 (51), 125 (78); Analysis: calcd. for $C_{15}H_{22}O_4$: C 67.65, H 8.33; found: C 67.81, H 8.39.

2,2'-Ethylidenebis[3-hydroxy-5,5-dimethylcyclohex-2-en-1-one] 73

A solution of 65 (162.7 mg, 0.774 mmol) and silica gel for flash chromatography (4 g) in CH_2Cl_2 (10 mL) was stirred at room temperature for 48 h. The reaction mixture was filtered and the solvent was removed in vacuo to give 73 (61.3 mg, 52%) as a pale yellow white solid. A portion of this was recrystallized from Skellysolve B to give 73 as white solid. Compound 73 has spectral properties identical with those reported in literature.[32] m.p.: 131-133°C; tlc: R_f 0.44 (1:3 ethyl acetate/ Skellysolve B); ftir (CH_2Cl_2, cast): 3500-2100 (br), 1599, 1581 cm^{-1}; uv (methanol) λ max: 259 (ε 22,376) nm; (methanol + 1 drop 10% NaOH): 282 (ε 28,912) nm; (methanol + 1 drop 10% NaOH + 3 drops 10% HCl): 258 (ε 24,750) nm; ^1H nmr (400 MHz, $CDCl_3$) δ: 12.51 (s, 1H, OH), 11.52 (brs, 1H, OH), 4.14 (q, 1H, J=7.5 Hz, $CH_3\underline{CH}$), 2.28 (m, 8H, 4 x CH_2), 1.49 (d, 3H, J=7.5 Hz, $\underline{CH_3}CH$), 1.05 (brs, 12H, 4 x CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 189.5 (s), 189.4 (s), 117.7 (s), 47.2 (t), 46.3 (t), 31.3 (s), 29.7 (q), 26.7 (q), 23.7 (d), 15.6 (q); hreims: m/z calcd. for $C_{18}H_{26}O_4$ (M^+): 306.1831; found: 306.1824 (88), 194 (37), 179 (100), 167 (58), 138 (43), 83 (62), 55

(32); Analysis: calcd. for $C_{18}H_{26}O_4$: C 70.56, H 8.55; found: C 70.77, H 8.55.

$\Delta^{1,10;3,8}$-5,5,9,13,13-Pentamethyl-2-oxatricyclo-[8.4.0^{1,10}0^{3,8}]tetradecan-7,11-dione 74

A solution of 73 (295.3 mg, 0.964 mmol) and p-toluenesulphonic acid-monohydrate (catalytic) in benzene (35 mL) was heated under reflux for 49 h. The solvent was removed in vacuo. The residue was purified by flash chromatography eluting with 1:4 ethyl acetate/Skellysolve B to give 74 (266.1 mg, 96%) as white crystals. A portion of this was recrystallized from benzene/Skellysolve B to afford 74 as white crystals. Compound 74 has spectral properties identical with those reported in the literature.[32] m.p.: 170-171°C; tlc: R_f 0.19 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1673, 1656 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 3.64 (q, 1H, J=6.5 Hz, $CH_3\underline{CH}$), 2.36 (s, 4H, 2 x CH_2), 2.27 (s, 4H, 2 x CH_2), 1.10 (s, 12H, 4 x CH_3), 1.09 (d, 3H, J=6.5 Hz, $\underline{CH_3}CH$); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 197.0 (s), 162.7 (s), 116.8 (s), 51.0 (t), 40.9 (t), 32.1 (s), 29.3 (q), 27.3 (q), 21.8 (q), 20.9 (d); hreims: m/z calcd. for $C_{18}H_{25}O_3$ (M^+): 288.1725; found: 288.1727 (5), 274 (19), 273 (100), 217 (18); Analysis: calcd. for $C_{18}H_{25}O_3$: C 74.97, H 8.39; found: C 74.63, H 8.41.

Irradiation of vinyl carbonate 65

A degassed solution of 65 (1.213 g, 6.18 mmol) in dry acetone (250 mL) was irradiated with a 450-W medium pressure mercury lamp through a Pyrex filter for 17 h. The reaction was monitored by tlc and irradiation was discontinued after the disappearance of ca. 70% of 65. The solvent was removed in vacuo. The residue was purified by flash chromatography eluting with 1:1 ethyl acetate/Skellysolve B. Four compounds, listed in order of elution, were obtained: unreacted 65 (339 mg, 28%), 79 (138 mg, 16%), 75 (72 mg, 8%), 76 (97 mg, 10%), and 80 (80 mg, 9%). Compounds 75 and 76 were converted (pyridine, Ac_2O, CH_2Cl_2, 4-DMAP) to the monoacetate derivatives 77 and 78, respectively, for easier characterization.

(1RS,6RS,7RS)-6,7-Carbonyldioxy-1-methylbicyclo-[4.2.0]octan-2-one 79

A portion of 79 was recrystallized from dichloromethane/Skellysolve B to afford 79 as colorless crystals. m.p.: 151-152°C; tlc: R_f 0.31 (1:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1805, 1707 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ : 4.75 (dd, 1H, J=4, 6.5 Hz, $CH_2\underline{CH}O$), 2.86 (dd, 1H, J=6.5, 14 Hz, $\underline{CH_2}CHO$), 2.47 (m, 2H), 2.16 (dd, 1H, J=4, 14.5 Hz, $\underline{CH_2}CHO$), 2.06 (m, 3H),

1.69 (m, 1H), 1.37 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, CD_2Cl_2) δ: 211.5 (s), 155.4 (s), 91.0 (s), 75.2 (d), 52.7 (s), 38.5 (t), 38.1 (t), 29.2 (t), 18.9 (t), 18.4 (q); hreims: m/z calcd. for $C_{10}H_{12}O_4$ (M^+): 196.0742; found: 196.0739 (48), 124 (91), 96 (60), 84 (100), 82 (74), 69 (51), 55 (64); Analysis: calcd. for $C_{10}H_{12}O_4$: C 61.22, H 6.16; found: C 61.16, H 6.25.

3-(1-Acetoxyethyl)-2-methylcyclohex-2-enone 77

Bulb to bulb distillation of 77 afforded 77 as a colorless oil. b.p.: 70°C/2 torr; tlc: R_f 0.26 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1742, 1671, 1635 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.72 (q, 1H, J=6.5 Hz, $CH_3\underline{CH}O$), 2.41 (m, 2H), 2.33 (m, 2H), 2.08 (s, 3H, CH_3CO_2), 1.95 (m, 2H), 1.83 (t, 3H, J=2 Hz, $CH_3C{=}C$), 1.35 (d, 3H, J=6.5 Hz, $\underline{CH_3}CHO$); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 199.1 (s), 170.0 (s), 155.2 (s), 130.6 (s), 70.1 (d), 37.8 (t), 24.4 (t), 22.4 (t), 20.9 (q), 17.9 (q), 10.2 (q); hreims: calcd. for $C_{11}H_{16}O_3$ (M^+): 196.1100; found: 196.1105 (47), 154 (52), 111 (100), 93 (31).

3-(1-Acetoxy-4-oxopentyl)-2-methylcyclohex-2-enone 78

Bulb to bulb distillation of 78 provided 78 as a colorless oil. b.p.: 106°C/1.8 torr; tlc: R_f 0.22 (1:1

ethyl acetate/Skellysolve B); ftir (film): 1741, 1717, 1669, 1630 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.59 (dd, 1H, J=5, 9.5 Hz, $CH_2\underline{CH}O$), 2.50 (m, 2H), 2.40 (m, 2H), 2.30 (m, 2H), 2.16 (s, 3H, CH_3CO_2), 2.08 (s, 3H, $CH_3C{=}O$), 1.95 (m, 4H); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 206.8 (s), 199.1 (s), 170.0 (s), 153.7 (s), 131.7 (s), 73.0 (d), 39.0 (t), 37.7 (t), 29.8 (q), 26.0 (t), 24.6 (t), 22.3 (t), 20.7 (q), 10.4 (q); hreims: m/z calcd. for $C_{14}H_{20}O_4$ (M^+): 252.1361; found: 252.1357 (10), 210 (23), 192 (76), 178 (57), 149 (33), 136 (55), 135 (100), 134 (76), 122 (31), 11 (43); Analysis: calcd. for $C_{14}H_{20}O_4$: C 66.65, H 7.99; found: C 66.63, H 7.79.

Spiro[(1SR,4RS)-4-methyl-[2]-oxa(2,1,1)hexan-3-one]-5,6'(RS)-[1]-oxahexan-2-one 80

A portion of 80 was recrystallized from dichloromethane/Skellysolve B to afford 80 as colorless crystals. m.p.: 158-159°C; tlc: R_f 0.16 (3:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1797, 1735 cm^{-1}; ^1H nmr (400 MHz, CD_2Cl_2) δ: 4.85 (d, 1H, J=1.5 Hz, CHO), 2.55 (m, 2H, $CH_2\underline{CH_2}C{=}O$), 2.28 (d, 1H, J=9.5 Hz, CH_2), 2.22 (dt, 1H, J=14.5 Hz, $\underline{CH_2}CH_2$), 2.18 (brd, 1H, J=9.5 Hz, CH_2, small coupling to δ4.85), 2.04 (ddd, 1H, J=5, 10.5, 14Hz, $\underline{CH_2}CH_2$), 1.94 (m, 2H, $\underline{CH_2}CH_2C{=}O$), 1.26 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, CD_2Cl_2) δ: 176.3 (s), 168.7 (s), 94.1

(s), 80.1 (d), 59.1 (s), 43.2 (t), 30.1 (t), 22.4 (t), 17.1 (t), 8.0 (q); Selective proton heteronuclear decouplings CH_3-C_4 (dq J=3, 127 Hz --> q J=127 Hz) upon [^{1}H] irradiation of δ 4.85 (H-1); hreims: m/z calcd. for $C_{10}H_{12}O_4$ (M^+): 196.0735; found: 196.0738 (0.07), 168 (9), 139 (31), 111 (31), 69 (100), 55 (43); Analysis: calcd. for $C_{10}H_{12}O_4$: C 61.22, H 6.16; found: C 61.13, H 6.24. For X-ray data see Figure 1 and reference 35.

4-Methyl-1,5-dihydroxybicyclo[3.3.0]octan-2-one 85

A solution of 79 (26.4 mg, 0.135 mmol) and excess potassium carbonate in a 1:1 MeOH/H_2O mixture (5 mL) was stirred overnight at room temperature. Most of the methanol was removed in vacuo and the residue was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated in vacuo to give 85 (22.3 mg, 97%) as a colorless oil. The ^{1}H nmr spectrum of 85 indicates that 85 exists as a mixture of 2 epimers in a 4:1 ratio. tlc: R_f 0.20 (1:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3433, 1743 cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$) δ : 3.45, 2.87 (2 brs, 2H, 2 OH), 2.55 (m, 2H), 2.26-1.66 (m, 7H), 1.18, 1.15 (2d, 3H, J=6.5 Hz, $\underline{CH_3}CH$, ratio 1:4); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 217.2 + 215.7 (s), 87.7 + 85.9 (s), 87.2 + 84.6 (s), 43.0 + 41.7 (t), 38.8 + 34.5 (d) 36.4 + 35.4 (t),

34.7 + 34.2 (t), 22.2 + 21.2 (t), 13.9 12.7 (q); hreims: m/z calcd. for $C_9H_{14}O_3$ (M^+): 170.0943; found: 170.0940 (88), 152 (24), 128 (52), 127 (100), 111 (51), 100 (93), 99 (65), 84 (78), 83 (35), 72 (33), 57 (84), 55 (87), 54 (30), 53 (57).

(1RS,6RS,8RS)-8-Methanesulfonyloxy-4,4,6-trimethyl-2-methylenebicyclo[4.2.0]octan-1-ol 87

Methanesulfonyl chloride (0.05 mL, 0.65 mmol) was added to a solution of 61 (82.0 mg, 0.42 mmol), triethylamine (0.12 mL, 0.86 mmol), and CH_2Cl_2 (3 mL) cooled to 0°C in an ice-water bath. The solution was stirred for 1 h at room temperature. Aqueous HCl (5%, 3 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 x 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford crude 87 (114.8 mg, 100%) as a yellowish white solid (m.p. 91-92°C dec.) which was used directly in the next reaction. Compound 87 decomposed on standing in air at room temperature but could be stored in a nitrogen filled flask in the fridge for up to six months with no decomposition. A portion of 87 was purified by recrystallization (diethylether/n-pentane) to afford 87 as white crystals. m.p.: 94-95°C (dec.); tlc: R_f 0.20 (1:3 ethyl acetate/Skellysolve B); ir (CCl_4): 3590, 3525,

1640, 1375, 1180 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$)δ : 5.16 (t, 1H, J=1.5 Hz, C=CH_2), 5.07 (t, 1H, J=8 Hz, $CH_2\underline{CH}O$), 4.92 (t, 1H, J=1.5 Hz, C=CH_2), 3.03 (s, 3H, CH_3SO_2), 2.24 (d, 1H, J=14 Hz, CH_2), 2.17 (d, 2H, J=8 Hz, $\underline{CH_2}CHO$), 2.10 (dd, 1H, J=3, 14 Hz, CH_2), 1.90 (s, 1H, OH), 1.69 (dd, 1H, J=3, 15 Hz, CH_2), 1.52 (d, 1H, J=15 Hz, CH_2), 1.17 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.85 (s, 3H, CH_3); hreims: calcd. for $C_{13}H_{22}O_4S(M^+)$: 274.1238; found: 274.1238 (0.1), 178 (5), 152 (100), 137 (77), 67 (24); Analysis: calcd. for $C_{13}H_{22}O_4S$: C 56.91, H 8.08; found: C 57.32, H 8.11.

(1RS,2SR,7RS)-5,5,7-Trimethyl-2-methylene-trans-bicyclo-[5.1.0]octan-2-ol 88

Lithium aluminum hydride (4.3 mg, 0.11 mmol) was added to a solution of 87 (27.0 mg, 0.10 mmol) in Et_2O (3 mL). After stirring for 1 h at room temperature, satd NH_4Cl (2 mL) was added and the reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography of the residue eluting with 1:9 diethyl ether/petroleum ether b.p. 30-60°C afforded 88 (11.5 mg, 65%) as a colorless oil; tlc: R_f 0.8 (1:1 diethyl ether/petroleum ether b.p. 30-60°C); ir ($CHCl_3$): 3595, 1635 cm^{-1}; ^1H nmr

(200 MHz, $CDCl_3$) δ: 5.20 (brt, 1H, J=1.5 Hz, C=CH_2), 4.97 (brs, 1H, $W_{\frac{1}{2}}$=5 Hz, C=CH_2), 4.94 (brs, 1H, $W_{\frac{1}{2}}$=9.4 Hz, C=CCHO), 2.37 (d, 1H, J=14 Hz, CH_2), 2.10 (d, 1H, J=14 Hz, CH_2), 1.76 (d, 1H, J=13 Hz, CH_2), 1.55 (brs, 1H, OH), 1.18 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 0.92 (dd, 1H, J=4, 9 Hz, H-8), 0.87 (d, 1H, J=13 Hz, CH_2), 0.79 (ddd, 1H, J=4.5, 8, 9 Hz, H-1), 0.73 (dd, 1H, J=4, 8 Hz, H-8); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ: 152.3, 111.2, 70.9, 52.2, 48.6, 41.2, 35.1, 30.2, 27.1, 22.8, 22.2, 16.8; hreims: m/z calcd. for $C_{12}H_{20}O_2$ (M^+): 180.1514; found: 180.1523 (7), 165 (27), 124 (36), 123 (77), 122 (39), 110 (34), 109 (84), 107 (62), 97 (53), 95 (80), 93 (46), 91 (39), 83 (44), 81 (68), 79 (43), 69 (55), 67 (60), 55 (100).

(1RS,7RS)-5,5,7-Trimethyl-2-methylene-trans-bicyclo-[5.1.0]octan-2-one 89

Pyridinium chlorochromate (34.6 mg, 16.1 mmol) was added to a solution of alcohol 88 (16.7 mg, 0.092 mmol) in CH_2Cl_2 (1 mL). After stirring for 20 min at room temperature the reaction mixture was diluted with Et_2O, and filtered through a fluorisil column. Concentration under reduced pressure followed by bulb to bulb distillation afforded 89 (13.5 mg, 82%) as a colorless oil: b.p.: 75°C/0.8 torr; tlc: R_f 0.46 (1:3 ethyl acetate/Skelly-

solve B); ir ($CHCl_3$): 1695, 1615 cm^{-1}; uv (methanol) λ max: 232 (ε 45,000) nm; ^1H nmr (400 MHz, $CDCl_3$) δ: 6.10 (d, 1H, J=1.5 Hz, $C=CH_2$), 5.23 (t, 1H, J=1.5 Hz, $C=CH_2$), 2.85 (brd, 1H, J=15 Hz, CH_2), 2.27 (dt, 1H, J=1.0, 8.5 Hz, H-1, small W coupling to δ 2.04), 2.25 (d, 1H, J=15 Hz, CH_2), 2.04 (brd, 1H, J=13 Hz, CH_2), 1.40 (d, 2H, J=8.5 Hz, two H-8 protons), 1.22 (d, 1H, J=13 Hz, CH_2), 1.13 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 0.96 (s, 3H, CH_3); hreims: m/z calcd. for $C_{12}H_{18}O(M^+)$: 178.1358; found: 178.1362 (6), 163 (15), 109 (76), 95 (45), 94 (100), 81 (40), 79 (53), 67 (74), 55 (36).

4,4-Dimethyl-6-methylene-2-(thiophenoxymethyl)cyclooctanone 90

Sodium hydride (6.2 mg, 0.129 mmol, 50% dispersion in oil) was rinsed three times with Skellysolve B under a nitrogen atmosphere. Dry HMPA (2 mL) and thiophenol (15 uL, 0.146 mmol) were added in succession. The mixture was stirred for 30 minutes at room temperature then a solution of 87 (6.8 mg, 0.025 mmol) in dry HMPA (0.5 mL) was added. The reaction mixture was heated at 75°C in an oil bath for 17 h. Water (3 mL) was added and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic extracts were washed with H_2O, satd NaCl, dried ($MgSO_4$), filtered, and concentrated to give a pale yellow oil.

Purification of this oil by flash chromatography eluting with 1:10 ethyl acetate/Skellysolve B furnished 90 (5.2 mg, 73%) as a colorless oil. tlc: R_f 0.46 (1:9 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3070, 1700, 1635 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 7.22 (m, 5H, ArS), 5.22 (brs, 1H, $C=CH_2$), 4.94 (brs, 1H, $C=CH_2$), 3.30 (dd, 1H, J=7, 13 Hz, CH_2S), 3.18 (dd, 1H, J=7.5, 13 Hz, CH_2S), 2.98 (m, 2H) 2.70 (brdd, 2H, J=5, 7.5 Hz, $\underline{CH_2}CH_2$), 2.42 (dt, 1H, J=5, 11.5 Hz, $\underline{CH_2}CH_2$), 2.21 (d, 1H, J=14 Hz, CH_2), 2.05 (dd, 1H, J=11.5, 15 Hz, $\underline{CH_2}CH$), 1.98 (d, 1H, J=14 Hz, CH_2), 1.82 (brd, 1H, J=15 Hz, $\underline{CH_2}CH$), 1.29 (s, 3H, CH_3), 1.18 (s, 3H, CH_3); hreims: calcd. for $C_{18}H_{24}SO$ (M^+): 288.1548; found: 288.1545 (100), 179 (31), 123 (61), 110 (50), 83 (39), 81 (40), 67 (33), 55 (65).

(1RS,7RS)-3-(Thiophenoxy methyl)-5,5,7-trimethyl-trans-bicyclo[5.1.0]octan-2-one 91

A solution of 87 (4.4 mg, 0.016 mmol) in dry HMPA (1 mL) was heated in an oil bath to 75°C for 17 h. Water (1 mL) was added and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic extracts were washed with H_2O, satd NaCl, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give after ptlc (1:3 ethyl acetate/Skellysolve B) unreacted 87 (1.5 mg, 34%) and 89 (0.8 mg, 33%, *vide supra*).

In a separate experiment n-butyllithium (1.18 M in hexane, 0.05 mL, 0.059 mmol) was added to a solution of thiophenol (13 uL, 0.127 mmol) in dry THF (1 mL) at room temperature under a nitrogen atmosphere. The mixture was stirred for 10 min then a solution of 89 (8.7 mg, 0.032 mmol) in dry THF (0.5 mL) was added. The mixture was stirred for 5 h at room temperature then satd NH_4Cl (2 mL) was added. The products were isolated by extraction with Et_2O (3 x 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give after ptlc (1:7 ethyl acetate/Skellysolve B) thiophenoxide 91 (7.4 mg, 85%) as a white solid. m.p.: 63-65°C; tlc: R_f 0.2 (1:9 ethyl acetate/Skellysolve B); ir (CCl_4): 3175, 1705 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 7.22 (m, 5H, ArS), 3.49 (dd, 1H, J=4, 13 Hz, CH_2S), 2.85 (dddd, 1H, J=4, 4.5, 8, 11.5 Hz, $\underline{CH}CH_2S$), 2.59 (dd, 1H, J=8, 13 Hz, CH_2S), 1.93 (d, 1H, J=13 Hz, CH_2), 1.84 (t, 1H, J=8.5 Hz, H-1), 1.71 (dd, 1H, J=4.5, 14.5 Hz, $\underline{CH_2}CH$), 1.58 (dd, 1H, J=11.5, 14.5 Hz, $\underline{CH_2}CH$), 1.33 (dd, 1H, J=5, 8.5 Hz, H-8), 1.27 (dd, 1H, J=5, 8.5 Hz, H-8) 1.19 (d, 1H, J=13.5 Hz, CH_2), 1.13 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.96 (s, 3H, CH_3); hreims: m/z calcd. for $C_{18}H_{24}SO$ (M^+): 288.1547; found: 288.1549 (100), 179 (75), 161 (31), 123.08 (46), 123.03 (74), 121 (34), 110 (56), 109.1 (40),

109.0 (30), 95 (61), 83 (53), 81 (47), 67 (36), 55.05 (84), 55.02 (36).

In a separate experiment sodium hydride (3.3 mg, 0.069 mmol, 50% dispersion in oil) was rinsed three times with Skellysolve B under a nitrogen atmosphere. Dry HMPA (0.5 mL) and thiophenol (11 uL, 0.107 mmol) were added in succession. The mixture was stirred for 30 min at room temperature then a solution of 91 (7.4 mg, 0.027 mmol) in dry HMPA (0.5 mL) was added. The reaction mixture was heated at 75°C in an oil bath for 17 h. Water (2 mL) was added and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic extracts were washed with H_2O, satd NaCl, dried ($MgSO_4$), filtered, and concentrated to give after ptlc (1:9 ethyl acetate/Skellysolve B) 90 (4.4 mg, 57%, vide supra) as a colorless oil.

(1RS,6RS,8RS)-8-(Methanesulfonyloxy)-4,4,6-trimethyl-2-methylene-1-trimethylsilyloxybicyclo[4.2.0]octane 92

A solution of 87 (75.3 mg, 0.274 mmol), hexamethyldisilizane (0.29 mL, 1.34 mmol), and dry trimethylsilylchloride (0.12 mL, 0.946 mmol) in dry DMSO (5 mL) was stirred at room temperature for 26 h. Water (5 mL) and ethyl acetate (10 mL) was added to the reaction mixture. The aqueous layer was extracted with additional ethyl acetate (2 x 20 mL). The organic layers were combined,

washed with 5% HCl (10 mL), satd $NaHCO_3$, satd NaCl, dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the residue by flash chromatography eluting with 1:9 ethyl acetate/Skellysolve B afforded 92 (88.9 mg, 93%) as a colorless oil which solidified in the fridge. m.p.: 36-38°C; tlc: R_f 0.42 (1:4 ethyl acetate/Skellysolve B); ftir (neat): 1645 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.15 (d, 1H, J=1.5 Hz, $C=CH_2$), 5.08 (t, 1H, J=6.5 Hz, $CH_2\underline{CH}O$), 4.97 (d, 1H, J=1.5 Hz, $C=CH_2$), 2.97 (s, 3H, CH_3SO_2), 2.10 (dd, 1H, J=7, 11.5 Hz, $\underline{CH_2}CHO$), 2.05 (d, 1H, J=14 Hz, $CH_2C=C$), 1.98 (brd, 1H, J=14 Hz, $CH_2C=C$), 1.94 (dd, 1H, J=6.5, 11.5 Hz, $\underline{CH_2}CHO$), 1.45 (brd, 1H, J=14.5 Hz, CH_2), 1.29 (d, 1H, J=14.5 Hz, CH_2), 1.12 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.16 (s, 9H, $(CH_3)_3Si$); hreims: m/z calcd. for $C_{16}H_{30}O_4SSi$ (M^+): 346.1634; found: 346.1639 (0.7), 250 (26), 224 (92), 209 (43), 153 (37), 75 (38), 73 (100).

(1RS,6RS,8RS)-1,8-Thiocarbonyldioxy-4,4,6-trimethyl-2-methylenebicyclo[4.2.0]octane 93

Chlorophenoxythioformate (0.05 mL, 0.36 mmol) was added to a stirred solution of diol 61 (55.9 mg, 0.28 mmol) and 4-N,N-dimethylaminopyridine (69.5 mg, 0.57 mmol) in CH_3CN (4 mL) at 0°C. After stirring for 18 h at room temperature the reaction mixture was quenched with satd

NaCl and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Purification of the residue by flash chromatography eluting with 1:19 ethyl acetate/Skellysolve B afforded 93 (38.1 mg, 56%) as a white solid (m.p. 71-73°C). A portion of this was recrystallized (diethyl ether/Skellysolve B) to afford 93 as colorless crystals. m.p.: 78-79°C; tlc: R_f 0.38 (1:3 ethyl acetate/Skellysolve B); ftir (CH_2Cl_2, cast): 1640, 1285 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$)δ : 5.22 (brs, 1H, $C=CH_2$), 5.09 (dd, 1H, J=5, 6.5 Hz, $CH_2\underline{C}HO$), 5.01 (brs, 1H, $C=CH_2$), 2.32 (dd, 1H, J=6.5, 13.5 Hz, $\underline{CH_2}CHO$), 2.19 (dd, 1H, J=2.5, 14 Hz, CH_2), 2.10 (d, 1H, J=14 Hz, CH_2), 2.05 (dd, 1H, J=5, 13.5 Hz, $\underline{CH_2}CHO$), 1.84 (dd, 1H, J=2.5, 15.5 Hz, CH_2), 1.57 (d, 1H, J=15.5 Hz, CH_2), 1.28 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); hreims: calcd. for $C_{13}H_{18}O_2S(M^+)$: 238.1028; found: 238.1039 (89), 240 ($M^+ + S^{34}$, 4), 178 (42), 150 (98), 135 (75), 121 (48), 107 (100), 94 (35), 93 (44), 91 (35), 79 (45), 67 (39), 55 (43); Analysis: calcd. for $C_{13}H_{18}O_2S$: C 65.51, H 7.61, S 13.45; found: C 65.41, H 7.53, S 13.59.

In a separate experiment a solution of diol 61 (23.1 mg, 0.118 mmol) and 1,1'-thiocarbonyldiimidazole (58.6 mg, 0.329 mmol) in 1,2-dichloroethane (3 mL) was heated under reflux for 8 h. The solvent was removed *in vacuo*.

Purification of the residue by flash chromatography eluting with 1:9 ethyl acetate/Skellysolve B afforded 93 (25.1 mg, 90%) as a white solid (m.p. 74-75°C).

(1SR,6RS,8RS)-4,4,6-Trimethyl-2-methylenebicyclo[4.2.0]-octan-8-ol 94

A solution of 93 (39.8 mg, 0.167 mmol) and azobisisobutyronitrile [catalytic] in dry benzene (2 mL) was heated under reflux while a solution of freshly distilled tributyltin hydride (64 uL, 0.231 mmol) in dry benzene (1 mL) was added by means of a syringe over 30 min. The reaction mixture was refluxed for an additional hour and then the organic solvent was removed by distillation in vacuo. Purification of the residue by flash chromatography eluting with 1:3 ethyl acetate/Skellsolve B gave 94 (23.6 mg, 78%) as white needles. m.p.: 56-58°C; tlc: R_f 0.32 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3585, 3525 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$)δ : 4.82 (t, 1H, J=2 Hz, C=CH_2), 4.68 (t, 1H, J=2 Hz, C=CH_2), 4.14 (brq, 1H, J=7.5 Hz, $CH_2\underline{CH}O$), 2.39 (d, 1H, J=7.5 Hz, $\underline{CH}CHO$), 2.15 (dd, 1H, J=7.5, 10.5 Hz, $\underline{CH_2}CHO$), 2.06 (brd, 1H, J=14 Hz, CH_2), 1.87 (dd, 1H, J=2, 14 Hz, CH_2), 1.86 (brs, 1H, OH), 1.52 (dd, 1H, J=7.5, 10.5 Hz, $\underline{CH_2}CHO$), 1.45 (dd, 1H, J=2, 14 Hz, CH_2), 1.37 (d, 1H, J=14.5 Hz, CH_2), 1.18 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.81 (s, 3H, CH_3);

hreims: m/z calcd. for $C_{12}H_{20}O_1(M^+)$: 180.1514; found: 180.1519 (0.2), 136 (100), 121 (57), 93 (27), 69 (79).

(1RS,6RS,8RS)-8-Acetoxy-4,4,6-trimethyl-2-methylene-bicyclo[4.2.0]octan-1-ol 95

A solution of 61 (144.5 mg, 0.74 mmol), pyridine (1.0 mL, 12.41 mmol) and acetic anhydride (0.40 mL, 4.20 mmol) in CH_2Cl_2 (7 mL) was stirred at room temperature for 23 h. HCl (5%, 5 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The organic layers were combined, washed with satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 95 (160.5 mg, 92%) as a yellowish white solid. A portion of this was recrystallized from Skellysolve B to give 95 as a white amorphous powder: m.p.: 63-65°C; tlc: R_f 0.32 (1:3 ethyl acetate/Skellysolve B); ir (CCl_4): 3590, 1740, 1645 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ : 5.20 (t, 1H, J=8 Hz, $CH_2\underline{CH}O$), 5.14 (brs, 1H, C=CH_2), 4.85 (brs, 1H, C=CH_2), 2.26 (brd, 1H, J=14 Hz, CH_2C=C), 2.25 (s, 1H, OH), 2.13 (dd, 1H, J=8, 11 Hz, $\underline{CH}_2CHO$), 2.11 (s, 3H, CH_3CO_2), 2.08 (brd, 1H, J=14 Hz, CH_2C=C), 1.94 (dd, 1H, J=8, 11Hz, $\underline{CH}_2CHO$), 1.60 (s, 2H, CH_2), 1.17 (s, 3H, CH_3), 0.97 (s, 3H, CH_3), 0.87 (s, 3H, CH_3); hreims: m/z calcd. for $C_{12}H_{20}O_2$ ($M^+ - C_2H_2O$, parent ion not seen): 196.1463; found: 196.1458 (4), 152 (100), 137 (77); Analysis:

calcd. for $C_{14}H_{22}O_3$: C 70.56, H 9.30; found: C 70.49, H 9.14.

(1RS,6RS,8RS)-1-Acetoxy-4,4,6-trimethyl-2-methylene-1-(trimethylsilyloxy)bicyclo[4.2.0]octane 96

A solution of 95 (154.5 mg, 0.65 mmol), hexamethyldisilizane (0.68 mL, 3.25 mmol), and dry trimethylsilyl chloride (0.41 mL, 3.25 mmol) in dry DMSO (4 mL) was stirred at room temperature for 5 h. Water (4 mL) and ethyl acetate (10 mL) were added to the reaction mixture. The aqueous layer was extracted with additional ethyl acetate (2 x 20 mL). The organic layers were combined, washed with 5% HCl (10 mL), satd $NaHCO_3$, satd NaCl, dried ($MgSO_4$), filtered, and concentrated in vacuo to afford 96 (150.2 mg, 75%) as a light yellow oil. A portion of this was purified by ptlc using 1:19 ethyl acetate/Skellysolve B to give pure 96 as a colorless oil. tlc: R_f 0.38 (1:19 ethyl acetate/Skellysolve B); ir (CCl_4): 1740, 1645 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 5.27 (dd, 1H, J=6, 7 Hz, $CH_2\underline{C}HO$), 5.19 (d, 1H, J=2 Hz, $C=CH_2$), 4.96 (d, 1H, J=2 Hz, $C=CH_2$), 2.11 (s, 3H, CH_3CO_2), 2.04 (brs, 2H, $CH_2C=C$), 2.04 (hidden dd, 1H, J=7.5, 11.5 Hz, $\underline{CH}_2CHO$), 1.65 (dd, 1H, J=6, 11 Hz, $\underline{CH}_2CHO$), 1.59 (s, 2H, CH_2), 1.13 (2s, 6H, 2 x CH_3), 0.16 (s, 9H, $(CH_3)_3Si$); hreims: m/z calcd. for

$C_{17}H_{30}Si_1O_3$ (M^+): 310.1964; found: 310.1966 (1.4), 250 (28), 224 (100), 209 (65), 73 (34).

6-(Ethanal)-4,4,6-trimethyl-2-methylenecyclohexanone 97

Diol 61 (21.2 mg, 0.11 mmol) was added to a stirred suspension of pyridinium chlorochromate (41.8 mg, 0.19 mmol) and sodium acetate trihydrate (16.8 mg, 0.20 mmol) in CH_2Cl_2 (1.5 mL) at room temperature. After stirring for twenty minutes the reaction mixture was diluted with Et_2O and filtered through a short fluorisil column. The organic extracts were concentrated under reduced pressure and subjected to bulb to bulb distillation to afford 97 (17.6 mg, 84%) as a colorless oil. b.p.: 58°C/1.0 torr; tlc: R_f 0.70 (1:1 diethyl ether/petroleum ether b.p. 30-60°C); ir ($CHCl_3$): 2720, 1715, 1685, 1610 cm^{-1}; ^1H nmr (100 MHz, $CDCl_3$) δ: 9.66 (t, 1H, J=1 Hz, $CH_2\underline{CH}O$), 5.98 (ddd, 1H, J=2, 2, 2 Hz, $C=CH_2$), 5.21 (ddd, 1H, J=2, 2, 2 Hz, $C=CH_2$), 2.91 (dd, 1H, J=1, 17 Hz, $\underline{CH_2}CHO$) 2.62 (dt, 1H, J=15, 2 Hz, CH_2), 2.54 (dd, 1H, J=1, 17 Hz, $\underline{CH_2}CHO$), 2.42 (dq, 1H, J=15, 2 Hz, CH_2), 1.83 (d, 1H, J=14 Hz, CH_2), 1.56 (dd, 1H, J=2, 14 Hz, CH_2), 1.25 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.00 (s, 3H, CH_3); hreims: m/z calcd. for $C_{10}H_{16}O_1$ ($M^+-C_2H_2O_1$, parent ion not seen): 152.1201; found: 152.1201 (100), 137 (72), 109.10 (32), 109.07 (30), 107 (43), 81 (36), 67 (62), 55 (71), 53 (34).

(1SR,6RS)-1-Hydroxy-4,4,6-trimethyl-2-methylenebicyclo-[4.2.0]octan-8-one 98

Dimethyl sulfoxide (0.11 mL, 1.55 mmol) was added by means of a syringe to a stirred solution of oxalyl chloride (53 uL, 0.608 mmol) in CH_2Cl_2 (2 mL) at -78°C under an atmosphere of nitrogen. After 10 min a solution of the diol 61 (98.9 mg, 0.504 mmol) in CH_2Cl_2 (1 mL) was added to the reaction mixture. After 15 min the reaction mixture was treated with triethylamine (0.35 mL, 2.51 mmol), then allowed to warm to room temperature (15 min). Water (3 mL) was added and the aqueous layer was extracted with additional CH_2Cl_2 (2 x 10 mL). The organic layers were combined, dried (Na_2SO_4), filtered, and concentrated to give a pale yellow oil. Purification of the oil by flash chromatography (1:5 ethyl acetate/Skellysolve B) furnished the following compounds listed in order of elution: 99 (6.4 mg, 5%), 100 (5.2 mg, 5%), 98 (68.8 mg, 70%), and 61 (20.4 mg, 21%).

Compound 99 has the following properties: tlc: R_f 0.54 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3070, 1775 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.25 (brs, 1H, C=CH_2), 5.18 (brs, 1H, C=CH_2), 4.89 (d, 1H, J=10.5 Hz, CH_2S), 4.61 (d, 1H, J=10.5 Hz, CH_2S), 3.01 (d, 1H, J=16.5 Hz, CH_2C=O), 2.21 (d, 1H, J=16.5 Hz, CH_2C=O),

2.18 (s, 3H, CH_3S), 2.05 (d, 1H, J=13 Hz, CH_2), 1.92 (dd, 1H, J=1.8, 13 Hz, CH_2), 1.61 (dd, 1H, J=1.8, 14.5 Hz, CH_2), 1.49 (d, 1H, J=14.5 Hz, CH_2), 1.19 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); hreims: m/z calcd. for $C_{14}H_{22}O_2S$ (M^+): 254.1340; found: 254.1337 (0.4), 193 (25), 61 (100).

Compound 100 has the following properties: tlc: R_f 0.40 (1:3 ethyl acetate/Skellysolve B); ftir (CH_2Cl_2, cast): 3500 (br), 3090 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.20 (t, 1H, J=2 Hz, C=CH_2), 4.78 (t, 1H, J=2 Hz, C=CH_2), 4.60 (d, 1H, J=11.5 Hz, CH_2S) 4.57 (d, 1H, J=11.5 Hz, CH_2S), 4.42 (t, 1H, J=8 Hz, $CH_2\underline{CH}O$) 2.85 (s, 1H, OH), 2.26 (d, 1H, J=13.5 Hz, CH_2), 2.15 (s, 3H, CH_3S), 2.07 (dd, 1H, J=3, 13.5 Hz, CH_2), 1.97 (dd, 1H, J=7.5, 11 Hz, $\underline{CH_2}CHO$), 1.83 (dd, 1H, J=8, 10.5 Hz, $\underline{CH_2}CHO$), 1.64 (dd, 1H, J=3, 14.5 Hz, CH_2), 1.54 (d, 1H, J=14.5 Hz, CH_2), 1.11 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.85 (s, 3H, CH_3); hreims: m/z calcd. for $C_{14}H_{24}O_2S$ (M^+): 256.1497; found: 256.1497 (0.7), 195 (19), 152 (100), 137 (43), 61 (91).

Compound 98 was distilled bulb to bulb to afford 98 as a colorless oil which solidified on standing. Compound 98 has the following properties: m.p.: 28-29°C; b.p.: 90°/0.4 torr; tlc: R_f 0.31 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3440, 3080, 1775, 1400, 1380 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.20 (dd, 1H, J=0.8, 2

Hz, C=CH_2), 5.10 (brs, 1H, C=CH_2), 3.03 (d, 1H, J=16.5 Hz, CH_2C=O), 2.42 (brs, 1H, OH), 2.27 (d, 1H, J=16.5 Hz, CH_2C=O), 2.12 (d, 1H, J=13.5 Hz, CH_2C=C), 1.98 (d, 1H, J=13.5 Hz, CH_2C=C), 1.66 (d, 1H, J=14 Hz, CH_2), 1.48 (d, 1H, J=14 Hz, CH_2), 1.16 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 207.6 (s), 142.7 (s), 116.8 (t), 87.5 (s), 52.1 (t), 44.3 (t), 43.2 (t), 35.5 (s), 33.2 (q), 32.2 (s), 26.9 (q), 24.6 (q); hreims: m/z calcd. for $C_{12}H_{18}O_2$ (M^+): 194.1306; found: 194.1304 (0.2), 152 (100), 137 (87), 109 (26), 95 (22); Analysis: calcd. for $C_{12}H_{18}O_2$: C 74.19, H 9.34; found: C 74.05, H 9.52.

(1SR,6RS)-1-Acetoxy-4,4,6-trimethyl-2-methylenebicyclo-[4.2.0]octan-8-one 104

A solution of triethylamine (0.36 mL, 2.58 mmol), acetic anhydride (0.22 mL, 2.33 mmol), 4-DMAP (1 crystal), and ketoalcohol 98 (335.7 mg, 1.73 mmol) in CH_2Cl_2 (5 mL) was stirred for 12 h at room temperature. Aqueous HCl (5%, 5 mL) was added. The aqueous layer was extracted with additional CH_2Cl_2 (2 x 15 mL). The organic layers were combined, washed with satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo to give a pale colored oil which was distilled bulb to bulb (80°C/0.4 torr) to give 104 (396.1 mg, 97%) as a colorless liquid. tlc: R_f

0.07 (1:19 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3075, 1790, 1743 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ : 5.36 (t, 1H, J=1.5 Hz, C=CH_2), 5.19 (brs, 1H, C=CH_2), 3.18 (d, 1H, J=17.5 Hz, CH_2C=O), 2.54 (d, 1H, J=17.5 Hz, CH_2C=O), 2.49 (brd, 1H, J=13.5 Hz, CH_2C=C), 2.07 (s, 3H, CH_3CO_2), 2.00 (brdd, 1H, J=1.2, 13.5 Hz, CH_2C=C), 1.76 (d, 1H, J=14 Hz, CH_2), 1.63 (dd, 1H, J=1.2, 14 Hz, CH_2), 1.21 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 0.98 (s, 3H, CH_3); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ : 201.5 (s), 169.3 (s), 139.7 (s), 120.0 (t), 90.6 (s), 54.1 (t), 45.7 (t), 44.8 (t), 37.3 (s), 33.3 (q), 31.8 (s), 27.9 (q), 25.0 (q), 20.9 (q); hreims: m/z calcd. for $C_{14}H_{20}O_3$ (M^+): 236.1412; found: 236.1406 (1.7), 194 (25), 152 (100), 137 (63), 109 (23), 55 (22); Analysis: calcd. for $C_{14}H_{20}O_3$: C 71.16, H 8.53; found: C 71.52, H 8.74.

(1SR,6RS)-1-Acetoxy-4,4,6-trimethyl-2-methylenebicyclo-[4.2.0]octan-8-one-p-toluene sulfonylhydrazone 106

A solution of 105 (116.2 mg, 0.492 mmol) and p-tosylhydrazine (109.5 mg, 0.588 mmol) in absolute EtOH (2 mL) was stirred at room temperature for 27 h. The solvent was removed in vacuo to give crude 106 (666.7 mg) which was used in the next step without further purification. A portion of impure 106 was recrystallized from MeOH to afford 106 as colorless needles: m.p.: 154-156°C; tlc:

R_f 0.17 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3200, 1725, 1600, 905, 810 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 9.10 (s, 1H, C=NH), 7.81 (d, 2H, J=8 Hz, ArH), 7.28 (d, 2H, J=8 Hz, ArH), 5.00 (brs, 1H, $C=CH_2$), 4.72 (brs, 1H, $C=CH_2$), 2.57 (d, 1H, J=14.5 Hz, $CH_2C=N$), 2.42 (d, 1H, J=14.5 Hz, $CH_2C=N$), 2.40 (s, 3H, CH_3Ar), 2.13 (s, 3H, CH_3CO_2), 2.10 (brd, 1H, J=13 Hz, $CH_2C=C$), 2.05 (dd, 1H, J=2, 13 Hz, $CH_2C=C$), 1.71 (dd, 1H, J=2, 14.5 Hz, CH_2), 1.62 (d, 1H, J=14.5 Hz, CH_2), 1.21 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 0.83 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 170.2 (s), 150.1 (s), 143.5 (s), 138.2 (s), 135.8 (s), 129.2 (2d), 128.1 (2d), 113.8 (t), 89.1 (t), 50.0 (t), 48.1 (t), 46.5 (t), 40.5 (s), 32.6 (s), 31.4 (q), 26.3 (q), 22.4 (q), 21.4 (q), 20.7 (q); hreims: m/z calcd. for $C_{19}H_{24}O_2N_2S$ ($M^+-C_2H_4O_2$, parent ion not seen); 344.1558; found: 344.1557 (11), 194 (12), 161 (11), 152 (100), 91 (30); Analysis: calcd. for $C_{21}H_{28}O_4N_2S$: C 62.35, H 6.98, N 6.92, S 7.93; found: C 62.23, H 7.21, N 6.79, S 7.78.

(1RS,6SR)-1-Acetoxy-4,4,6-trimethyl-2-methylenebicyclo-[4.2.0]octane 26

A solution of 106 (140.6 mg, 0.348 mmol) in dry $CHCl_3$ (3 mL) was cooled to 0°C in an ice-water bath and catecholborane (0.04 mL, 0.487 mmol) was added by means of a syringe. The hydroboration reaction was allowed to

proceed for 1 h at 0°C then MeOH (4 drops) was added to destroy excess reagent. Sodium acetate trihydrate (265 mg, 1.95 mmol) and DMSO (2 mL) were added and the reaction mixture was heated under gentle reflux for 1 h. $CHCl_3$ (10 mL) was added and the organic extract was washed with 5% NaOH (2 x 5 mL), H_2O (5 mL), and satd NaCl. The organic extract was dried ($MgSO_4$), filtered, and concentrated at atmospheric pressure to give a pale yellow oil. Purification of this oil by flash chromatography using 1:19 ethyl acetate/Skellysolve B [the solvents were removed by distillation at atmospheric pressure] furnished 26 (20.4 mg, 26%) as a colorless liquid. tlc: R_f 0.27 (1:19 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3090, 1745 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.26 (brd, 1H, J=2 Hz, $C=CH_2$) 5.01 (brt, 1H, J=2 Hz, $C=CH_2$), 2.55 (ddd, 1H, J=3, 8.5, 12.5 Hz, $\underline{CH_2}CH_2$), 2.33 (dt, 1H, J=12.5, 10 Hz, $\underline{CH_2}CH_2$), 2.04 (brd, 1H, J=13.5 Hz, CH_2), 1.90 (s, 3H, CH_3CO_2), 1.87 (d, 1H, J=13.5 Hz, CH_2), 1.67 (dt, 1H, J=8.5, 10.5 Hz, $CH_2\underline{CH_2}$), 1.35 (dt, 1H, J=3, 10.5 Hz, $CH_2\underline{CH_2}$), 1.24 (d, 1H, J=14 Hz, CH_2), 1.20 (d, 1H, J=14 Hz, CH_2), 1.09 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ: 172.4 (s), 144.7 (s), 115.4 (t), 86.0 (s), 47.4 (t), 44.8 (t), 44.1 (s), 33.3 (q), 32.0 (s), 29.8 (t), 28.0 (q), 27.6 (t), 25.4 (q), 21.7 (q); hreims: m/z calcd. for $C_{14}H_{22}O_2(M^+)$:

222.1620; found: 222.1613 (2), 180 (100), 162 (24), 152 (44), 147 (36), 109 (32), 55 (45).

(1RS,6RS,8RS)-1,8-Carbonyldioxy-2,4,4,6-tetramethyl-bicyclo[4.2.0]oct-2-ene 108

A solution of alkene carbonate 62 (206.0 mg, 0.926 mmol) and rhodium(III) chloride trihydrate (catalytic amount) in absolute 2-propanol (5 mL) was heated under reflux for 4 days. Rhodium(III) chloride trihydrate (catalytic amount) was added to the reaction mixture each time the color disappeared. Water (5 mL) and CH_2Cl_2 (20 mL) was added. The aqueous extracts were extracted with CH_2Cl_2 (2 x 20 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash chromatography with 1:9 ethyl acetate/Skellysolve B to afford 108 (150.0 mg, 73%) as a colorless oil.

In a separate experiment ketocarbonate 25 (101.1 mg, 0.45 mmol) in dry THF (4 mL) was cooled to -78°C in a dry ice-acetone bath. Methyl lithium (0.41 ml, 0.49 mmol, 1.2 M in diethyl ether) was added by means of a syringe and the resulting solution was stirred at -78°C for 0.5 h. Dry pyridine (0.07 mL, 0.87 mmol) and thionyl chloride (0.07 mL, 0.96 mmol) were then added separately by means of a syringe. The resulting solution was allowed to warm

to room temperature and stirred for 2 h. Water (5 mL) and CH_2Cl_2 (20 mL) was added. The aqueous extracts were extracted with CH_2Cl_2 (2 x 20 mL). The organic extracts were combined, washed with 5% HCl, satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash chromatography using 1:9 ethyl acetate/Skellysolve B to afford 108 (77.9 mg, 78%) as a colorless oil. tlc: R_f 0.19 (1:9 ethyl acetate/Skellysolve B); ftir (neat): 1809 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 5.70 (d, 1H, J=1.5 Hz, C=CH), 4.68 (dd, 1H, J=3, 6 Hz, CH_2CHO), 2.36 (dd, 1H, J=6, 14 Hz, CH_2CHO), 1.98 (dd, 1H, J=3, 14 Hz, CH_2CHO), 1.70 (d, 3H, J=1.5 Hz, $CH_3C=C$), 1.61 (s, 2H, CH_2), 1.34 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 1.06 (s, 3H, CH_3); hreims: m/z calcd. for $C_{13}H_{18}O_3$ (M^+): 222.1256; found: 222.1257 (14), 207 (6), 166 (100), 163 (66), 149 (34), 122 (86), 119 (47), 110 (42), 107 (51), 94 (37), 91 (34), 79 (33), 67 (45).

(1RS,6RS,8RS)-1,8-Carbonyldioxy-2-methylenebicyclo[4.2.0]-octane 111

n-Butylithium (1.20 mL, 1.41 mmol, 1.17 M solution in hexane) was added to a stirred suspension of methyltriphenylphosphonium bromide (646.7 mg, 1.81 mmol) in dry THF (20 mL) cooled to 0°C in an ice-water bath. The solution was stirred for 15 min then cooled to -78°C in a

dry ice-acetone bath. A solution of ketone 66 (256.1 mg, 1.40 mmol) in dry THF (1 mL) was added by means of a syringe and the solution was allowed to warm to room temperature with stirring over a 2 h period. Water (5 mL) was added, THF was removed *in vacuo*, and the reaction mixture was extracted with CH_2Cl_2 (3 x 35 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Separation of the residue by flash chromatography using 1:4 ethyl acetate/Skellysolve B afforded in order of elution: 111 (210.9 mg, 83%) as a colorless oil and diol 112 (9.7 mg, 5%, *vide infra*). A small amount of 111 was purified by bulb to bulb distillation to give 111 as a colorless oil which solidifies on standing. m.p. 40-42°C; b.p.: 75°C/1 torr; tlc: R_f 0.23 (1:4 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3090, 1805, 1643 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.19 (brs, 1H, $C=CH_2$), 5.09 (brs, 1H, $C=CH_2$), 4.90 (dd, 1H, J=4, 6 Hz, $CH_2\underline{CH}O$), 2.81 (ddt, 1H, J=5, 9.5, 7 Hz, $\underline{CH}CH_2$), 2.47 (m, 1H), 2.44 (ddd, 1H, J=4, 9.5, 14 Hz, $\underline{CH_2}CHO$), 2.32 (m, 1H), 2.17 (ddd, 1H, J=5, 6.5, 14 Hz, $\underline{CH_2}CHO$), 2.05 (m, 1H), 1.70 (m, 1H), 1.54 (m, 1H), 1.45 (m, 1H); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ: 155.9 (s), 140.8 (s), 113.1 (t), 86.6 (s), 78.6 (d), 39.0 (d), 32.7 (t), 31.4 (t), 29.6 (t), 21.5 (t); hreims: m/z calcd. for $C_{10}H_{12}O_3(M^+)$: 180.0786; found: 180.0782 (16),

152 (37), 126 (40), 107 (41), 93 (45), 91 (38), 80 (38), 79 (100); Analysis: calcd. for $C_{10}H_{12}O_3$: C 66.65, H 6.71; found: C 66.48, H 6.72.

(1RS,6RS,8RS)-2-Methylenebicyclo[4.2.0]octane-1,8-diol 112

A solution of carbonate 111 (454.8 mg, 2.52 mmol) and excess potassium carbonate in 1:1 MeOH/H_2O (10 mL) was stirred at room temperature for 12 h. The reaction mixture was concentrated in vacuo and the aqueous residue was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 112 (387.0 mg, 99%) as pale yellow needles (m.p. 57-59°C). A portion of this was recrystallized from diethyl ether/Skellysolve B to give 112 as colorless needles: m.p.: 63-64°C; tlc: R_f 0.20 (1:1 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3261, 1647 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ : 5.08 (s, 1H, $C=CH_2$), 4.97 (d, 1H, J=1.5 Hz, $C=CH_2$), 4.33 (t, 1H, J=6 Hz, $CH_2\underline{CH}O$), 3.48, 3.14 (2 brs, 2H, 2 x OH), 2.37 (m, 1H), 2.28 (m, 1H, $\underline{CH}CH_2$), 2.21 (m, 1H), 2.04 (ddd, 1H, J=6, 9, 11.5 Hz, $\underline{CH_2}CHO$), 1.96 (m, 1H), 1.86 (ddd, 1H, J=5, 6, 11.5 Hz, $\underline{CH_2}CHO$), 1.64 (m, 1H), 1.39 (m, 2H); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ : 149.0 (s), 109.8 (t), 76.6 (s), 70.0 (d), 38.7 (d), 32.9 (2t), 29.4 (t), 23.7 (t); hreims: m/z calcd. for $C_9H_{14}O_2(M^+)$: 154.0994; found: 154.0991 (0.4),

110 (56), 95 (100); Analysis: calcd. for $C_9H_{14}O_2$: C 70.10, H 9.15; found: C 69.84, H 9.09.

(1RS,7RS)-3-Methylene-trans-bicyclo[5.1.0]octan-2-one 110

Methanesulfonyl chloride (1.22 mL, 15.45 mmol) was added to a solution of diol 112 (1.356 g, 8.79 mmol) and pyridine (1.45 mL, 17.93 mmol) in CH_2Cl_2 (15 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred at 0°C for 5 h then 5% HCl (10 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL), the organic layers combined, washed with satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was passed through a silica gel column (super 1 alumina-Type W 200-basic aluminum oxide) using 1:3 ethyl acetate/Skellysolve B to afford trans-110 (915 mg, 76%) as an almond-smelling, yellowish, clear liquid. ^1H nmr analysis indicates a small amount (ca. 3%) of the cis-isomer was present. b.p.: 65°C/ water aspirator vacuum; tlc: R_f 0.35 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1700, 1615 cm^{-1}; ^1H nmr (400 MHz, C_6D_6) δ : 6.15 (dd, 1H, J=1.5, 2.5 Hz, C=CH_2), 4.99 (t, 1H, J=2.5 Hz, C=CH_2), 2.27 (ddd, 1H, J=2.5, 5.5, 15 Hz, CH_2C=C), 2.21 (m, 1H, CH_2C=C), 1.82 (ddt, 1H, J=4.5, 13, 2.8 Hz, CH_2CH), 1.74 (dddd, 1H, J=2.8, 4.5, 6.5, 14 Hz, CH_2CH_2), 1.57 (dt, 1H, J=5.5, 7.5 Hz, H-8), 1.34 (m, 1H), 1.31

(apparent dt, 1H, J=6.5, 7.5 Hz, H-1), 0.88 (dt, 1H, J=5.5, 6.5 Hz, H-8), 0.52 (ddt, 1H, J=4, 11.5, 13 Hz, $\underline{CH_2}CH$), 0.07 (dddt, 1H, J=2.8, 6.5, 11.5, 7.5 Hz, H-7); Note: Signals corresponding to H-1 and the two H-8 protons could not be conclusively assigned from double irradiation experiments. They were readily assigned from selective proton heteronuclear decoupling experiments after the multiplicities of all the ^{13}C signals were determined by gated spin-echo experiments (GASPE)[65]. The coupling constant between H-1 and H-7 is determined to be 7.5 Hz. ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 193.8 (s), 149.3 (s), 120.8 (t), 34.7 (t), 32.5 (2t), 32.0 (d, C-1), 25.5 (d, C-7), 16.7 (t, C-8); hreims: m/z calcd. for $C_9H_{12}O(M^+)$: 136.0888; found: 136.0888 (50), 93 (73), 80 (100), 79 (98), 78 (60), 77 (33), 67 (67), 55 (59), 53 (34).

Nuclear Overhauser enhancement difference spectroscopy (nOeds) on 110 gave the following results: presaturation of H-7 (δ 0.07): 0% (H-1); presaturation of H-8 (δ 1.57): 4% (H-7), 14% (H-8, δ 0.88), 0% (H-1).

(1RS,2RS,7RS)-3-Methylene-trans-bicyclo[5.1.0]octan-2-ol 114

A solution of 110 (31.9 mg, 0.234 mmol), ceric chloride trihydrate (0.6 mL, 0.24 mmol, 0.4 M in MeOH),

sodium borohydride (9.0 mg, 0.233 mmol) and dry MeOH (1 mL) was stirred at room temperature for 30 min. Satd NH_4Cl (4 drops) was added and the solvent was removed *in vacuo* and the residue was extracted with Et_2O (2 x 20 mL). The combined organic extracts were washed with H_2O, satd NH_4Cl, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give **114** (28.0 mg, 63%) as a colorless oil. A portion of this was subjected to bulb to bulb distillation to give **114** as a colorless oil. b.p.: 50°C/0.5 torr; tlc: R_f 0.42 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3390, 3025, 1630 cm^{-1}; ^1H nmr (400 MHz, C_6D_6) δ: 5.07 (brs, 1H, C=CH_2), 4.88 (brs, 1H, C=CH_2), 4.45 (brs, 1H, $W_{\frac{1}{2}}$=6.5 Hz, C=CCHO), 2.26 (ddd, 1H, J=2.3, 7.5, 14 Hz, CH_2C=C), 1.96 (m, 2H), 1.80 (m, 1H), 1.65 (m, 1H), 1.44 (s, 1H, OH), 1.02 (ddd, 1H, J=5, 7.5, 8 Hz, H-8), 0.74 (ddd, 1H, J=5, 7.5, 8 Hz, H-8), 0.65 (ddt, 1H, J=6, 9, 11.5 Hz, CH_2CH), 0.50 (dddt, 1H, J=3.5, 8, 11.5, 7.5 Hz, H-7), 0.15 (dq, 1H, J=3.5, 8 Hz, H-1); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 157.6 (s), 111.7 (t), 69.6 (d), 34.5 (t), 34.1 (t), 30.2 (t), 22.7 (d, C-1), 13.5 (d, C-7), 13.1 (t, C-8); hreims: m/z calcd. for $C_9H_{14}O(M^+)$: 138.1045; found: 138.1041 (1.7), 120 (3), 95 (100), 84 (61), 83 (30), 79 (48), 67 (59); Analysis: calcd. for $C_9H_{14}O$; C 78.21, H 10.21; found: C 78.48, H 10.25.

(1RS,2RS,7RS)-3-Methylene-2-[(phenylcarbamoyl)oxy]-trans-bicyclo[5.1.0]octane 115

A solution of 114 (50.5 mg, 0.365 mmol) and phenyl isocyanate (15 drops) in CH_2Cl_2 (2 mL) was stirred at room temperature for 24 h. 10% HCl (8 drops) was added and the aqueous layer was extracted with CH_2Cl_2 (2 x 10 mL). The organic extracts were combined, washed with satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash chromatography of the residue eluting with 1:9 ethyl acetate/Skellysolve B gave 115 (58.3 mg, 57%) as a colorless solid. A portion of this was recrystallized from n-pentane/diethyl ether to give 115 as colorless needles. m.p.: 106-107°C; tlc: R_f 0.26 (1:9 ethyl acetate/Skellysolve B); ^1H nmr (400 MHz, $CDCl_3$) δ: 7.38 (brd, 2H, J=7.5 Hz, ArH), 7.30 (t, 2H, J=7.5 Hz, ArH), 7.05 (t, 1H, J=7.5 Hz, ArH), 6.58 (brs, 1H, NH), 5.71 (d, 1H, J=3.8 Hz, C=CCHO), 5.02 (brs, 1H, $C=CH_2$), 5.00 (brs, 1H, $C=CH_2$), 2.43 (ddd, 1H, J=2.5, 7.0, 14 Hz, $CH_2C=C$), 2.25 (ddd, 1H, J=2.5, 11, 14 Hz, $CH_2C=C$), 2.11 (m, 1H), 2.05 (m, 1H), 1.81 (m, 1H), 0.97 (hidden dt, 1H, J=5.5, 7.5 Hz, H-8), 0.94 (hidden dt, 1H, J=5.5, 7.5 Hz, H-8), 0.88 (m, 1H), 0.57 (dq, 1H, J=3.8, 7.5 Hz, H-1), 0.47 (ddq, 1H, J=3.2, 11, 7.5 Hz, H-7); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 152.9 (s), 152.6 (s), 137.9 (s), 129.0 (2d),

123.4 (2d), 118.6 (d), 113.0 (t), 72.8 (d), 34.4 (t), 34.3 (t), 30.1 (t), 21.0 (d), 15.0 (d), 13.9 (t); hreims: m/z calcd. for $C_{16}H_{19}O_2N(M^+)$: 257.1415; found: 257.1410 (7), 121 (100), 79 (99), 67 (52); Analysis: calcd. for $C_{16}H_{19}O_2N$: C 74.68, H 7.44; N 5.44; found: C 74.77, H 7.59, N 5.37. For X-ray structure determination see Figure 2 and reference 68.

(1SR,7RS)-3-(Benzenethiomethyl)-cis-bicyclo[5.1.0]octan-2-one 121 and (1RS,3SR,7RS)-3-(Benzenethiomethyl)-trans-bicyclo[5.1.0]octan-2-one 119 and (1RS,3RS,7RS)-3-(Benzenethiomethyl)-trans-bicyclo[5.1.0]octan-2-one 120

A solution of 110 (510.3 mg, 3.75 mmol), triethylamine (1.05 mL, 7.53 mmol), thiophenol (0.58 mL, 5.65 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 48 h. 5% HCl (10 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (2 x 20 mL). The organic extracts were combined, washed with satd $NaHCO_3$, dried (Na_2SO_4), filtered and concentrated in vacuo. Flash chromatography of the residue using 1:49 acetone/benzene afforded in order of elution: 121 (31.8 mg, 3.4%) and an inseparable mixture (1:1) of 119 and 120 (506.0 mg, 55%). Compounds 119 and 120 could be separated on a silica gel column (Mn Kieselgel 60-200 mesh) using benzene as eluent. Analytical samples of 119, 120, and 121 were prepared by

bulb to bulb distillation under reduced pressure. Compound 121 displays the following properties; b.p.: 90°C/0.2 torr; tlc: R_f 0.45 (1:49 acetone/benzene); ftir ($CHCl_3$, cast): 3075, 1704 cm^{-1}; ^1H nmr (400 MHz, C_6D_6) δ: 7.30 (dt, 2H, J=1.5, 7.0 Hz, ArS), 7.03 (tt, 2H, J=1.5, 7.0 Hz, ArS), 6.93 (tt, 1H, J=1.5, 7.0 Hz, ArS), 3.39 (m, 1H, CH_2S), 2.77 (m, 2H), 1.91 (dt, 1H, J=5.5, 15.5 Hz, $\underline{CH_2}CH$), 1.56 (dq, 1H, J=13.5, 3.5 Hz, $\underline{CH_2}CH_2$), 1.48 (ddd, 1H, J=5.5, 7.5, 10.5 Hz, H-1), 1.35 (m, 1H), 0.97 (apparent dt, 1H, J=5, 5.5 Hz, H-8), 0.85 (dq, 1H, J=3, 12.5 Hz, $\underline{CH_2}CH_2$), 0.71 (dq, 1H, J=12.5, 3.5 Hz, $\underline{CH_2}CH_2$), 0.58 (dt, 1H, J=5, 7.5 Hz, H-8), 0.46 (ddt, 1H, J=7.5, 5.5, 10.5 Hz, H-7), 0.21 (dt, 1H, J=15.5, 10.5 Hz, $\underline{CH_2}CH$). The coupling constant between H-1 and H-7 was determined to be 10.5 Hz. ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 208.5 (s), 136.5 (s), 129.6 (2d), 129.0 (2d), 126.2 (d), 54.1 (d), 35.2 (t), 33.2 (t), 30.4 (t), 29.4 (d, C-1), 26.9 (t), 14.3 (d, C-7), 12.3 (t, C-8); hreims: m/z calcd. for $C_{15}H_{18}OS(M^+)$: 246.1078; found: 246.1088 (45), 137 (25), 67 (39), 55 (100); Analysis: calcd. for $C_{15}H_{18}OS$: C 73.13, H 7.36; found: C 73.12, H 7.40. Nuclear Overhauser enhancement difference spectroscopy (nOeds) on 121 gave the following results: presaturation at H-1 (δ 1.48): 7% (H-7); presaturation at H-7 (δ 0.46): 13% (H-1).

Compound 119 displays the following properties: b.p.: 155°C/2.5 torr; tlc: R_f 0.21 (1:49 acetone/benzene); ftir ($CHCl_3$, cast): 3055, 1698 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 7.33 (dd, 2H, J=1.5, 7.5 Hz, ArS), 7.26 (dt, 2H, J=1.5, 7.5 Hz, ArS), 7.15 (tt, 1H, J=1.5, 7.5 Hz, ArS), 3.61 (m, 1H, CH_2S), 2.73 (dd, 1H, J=9, 12.5 Hz, CH_2S), 2.70 (m, 1H, $\underline{CH}CH_2S$), 2.11 (m, 2H), 1.99 (m, 1H), 1.86 (apparent ddd, 1H, J=5.5, 7.5, 8.0 Hz, H-8), 1.78 (dddd, 1H, J=1, 7, 10, 14 Hz, $\underline{CH_2}CH_2$), 1.70 (m, 1H), 1.61 (dt, 1H, J=6.5, 7.5 Hz, H-1), 1.27 (dt, 1H, J=5.5, 6.5 Hz, H-8), 1.17 (dddd, 1H, J=4.5, 7, 11, 13.5 Hz, $\underline{CH_2}CH$), 0.53 (ddddd, 1H, J=5.5, 6.5, 7.5, 8.0, 11.0 Hz, H-7); J (H-1, H-7)=7.5 Hz; ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 205.0 (s), 136.6 (s), 128.9 (2d), 128.8 (2d), 125.8 (d), 53.2 (d), 33.8 (t), 30.0 (d, C-1), 28.7 (t), 27.4 (t), 26.4 (t), 24.6 (d, C-7), 18.7 (t, C-8); hreims: m/z calcd. for $C_{15}H_{18}OS(M^+)$: 246.1079; found: 246.1077 (30), 137 (6), 67 (54), 55 (100); Analysis: calcd. for $\underline{C_{15}H_{18}OS}$: C 73.13, H 7.36; found: C 72.92, H 7.32.

Compound 120 displays the following properties: b.p.: 145°C/1.3 torr; ftir ($CHCl_3$, cast): 3060, 1703 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 7.37 (dt, 2H, J=6.5, 1.5 Hz, ArS), 7.27 (tt, 2H, J=1.5, 6.5 Hz, ArS), 7.17 (tt, 1H, J=1.5, 6.5 Hz, ArS), 3.37 (dd, 1H, J=3.5, 13 Hz, CH_2S), 3.06 (dd, 1H, J=8.5, 13Hz, CH_2S), 2.68 (ddt, 1H, J=3.5,

11.5, 7.0 Hz, CHCH$_2$S); 2.20 (m, 3H), 1.91 (m, 1H), 1.78 (apparent dt, 1H, J=6.5, 8.0 Hz, H-1), 1.72 (dt, 1H, J=5.5, 8.0 Hz, H-8), 1.59 (m, 1H), 1.28 (dt, 1H, J=5.5, 6.5 Hz, H-8), 1.01 (dt, 1H, J=3.5, 12.5 Hz, CH$_2$CH), 0.36 (ddq, 1H, J=3.5, 6.5, 8.0 Hz, H-7); J (H-1, H-7)=8.0 Hz; ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 204.9 (s), 136.3 (s), 129.5 (2d), 129.0 (2d), 126.2 (d), 53.9 (d), 37.9 (t), 32.1 (t), 31.9 (d, C-1), 30.6 (t), 30.4 (t), 25.1 (d, C-7), 16.8 (t, C-8); hreims: m/z calcd. for $C_{15}H_{18}OS$ (M^+): 246.1078; found: 246.1075 (13), 137 (23), 55 (100); Analysis: calcd. for $C_{15}H_{18}OS$: C 73.13, H 7.36; found: C 73.16, H 7.32.

(1SR,7RS)-3-(Phenylsulfinylmethyl)-cis-bicyclo[5.1.0]-octan-2-one 123

A solution of m-chloroperbenzoic acid (103.4 mg, 0.600 mmol, buffer washed) in CH_2Cl_2 (5 mL) was added to a solution of 121 (143.4 mg, 0.582 mmol) in CH_2Cl_2 (20 mL) cooled to 0°C in an ice-water bath. The reaction mixture was stirred at room temperature for 1 h and then satd $NaHCO_3$ (10 mL) was added. The aqueous layer was extracted with additional CH_2Cl_2 (3 x 20 mL), the organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated in vacuo. Flash chromatography of the residue eluting with 1:1 ethyl acetate/Skellysolve B afforded 122 (150.4

mg, 99%) as a light yellow oil. ^{1}H and ^{13}C nmr analysis indicate that 122 exists as a 1:1 mixture of diastereomers presumably isomeric at sulfur. tlc: R_f 0.15 (1:1 ethyl acetate/Skellysolve B); ftir (film): 3055, 1700, 1040 cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$) δ: 7.58 (m, 5H), 3.40 (m, 2H), 2.82, 2.62 (m, 1H), 2.26 (m, 1H), 2.03 (m, 1H), 1.76 (m, 2H), 1.40 (m, 1H), 1.17 (m, 1H), 0.99 (m, 2H), 0.84 (m, 1H), 0.37 (m 1H); ^{13}C nmr (50.3 MHz, $CDCl_3$)δ : 207.4 + 206.8 (s), 143.5 + 144.5 (s), 131.0 + 130.8 (2d), 129.2 + 129.2 (2d), 124.1 + 123.7 (d), 60.0 + 58.3 (t), 48.1 + 46.5 (d), 33.5 + 33.1 (t), 30.3 + 30.2 (t), 28.9 + 28.4 (d, C-1), 26.6 + 26.5 (t), 14.3 + 14.2 (d, C-7), 12.3 + 12.1 (t, C-8); hreims: m/z calcd. for $C_{15}H_{18}O_2S$ (M^+): 262.1027; found: 262.1035 (4), 137 (90), 67 (35), 55 (100).

(1SR,7RS)-2-Methylene-cis-bicyclo[5.1.0]octan-2-one 113

A solution of 122 (55.1 mg, 0.21 mmol) and dry benzene (10 mL) was heated under reflux for 10 h. Most of the solvent was removed by heating in a water bath (T=75°C). Flash chromatography of the residue using 1:40 acetone/benzene gave 113 (12.5 mg, 44%) as a light yellow liquid. Bulb to bulb distillation gave 113 (4.5 mg, 16%) as a colorless liquid: b.p.: 100°C/721 torr; tlc: R_f 0.35 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$,

cast): 1700 cm^{-1}; ^1H nmr (400 MHz, acetone-$\underline{d}_6$) δ: 5.48 (d, 1H, J=2.5 Hz, C=CH_2), 5.13 (brs, 1H, C=CH_2), 2.41 (m, 2H), 1.88 (dt, 1H, J=5.5, 9 Hz, H-1), 1.86 (m, 1H), 1.51 (m, 1H), 1.38 (hidden dddt, 1H, J=3.3, 6.5, 9, 8 Hz, H-7), 1.36 (m, 2H), 0.99 (ddd, 1H, J=5, 8, 9 Hz, H-8), 0.66 (dt, 1H, J=5, 5.5 Hz, H-8); J (H-1, H-7): 9 Hz; ^{13}C nmr (100.6 MHz, acetone-$\underline{d}_6$) δ: 203.6 (s), 150.0 (s), 119.5 (t), 32.1 (t), 27.8 (t), 27.3 (d), 26.7 (t), 16.7 (d), 11.3 (t); hreims: m/z calcd. for $C_9H_{12}O$ (M^+): 136.0889; found: 136.0889 (14), 80 (55), 79 (80), 67 (70), 55 (100), 54 (40), 53 (39); Nuclear Overhauser enhancement difference spectroscopy (n0eds) on 113 gave the following results: presaturation at H-8 (δ 0.99): 6.9% (H-7), 5.3% (H-1), ~23% (other H-8, δ 0.66); presaturation at H-8 (δ 0.66): 0% (H-7), 0% (H-7), 25% (H-8, δ 0.99).

(1RS,3SR,7RS)-3-Methyl-trans-bicyclo[5.1.0]octan-2-one 123 and (1RS,3RS,7RS)-3-Methyl-trans-bicyclo[5.1.0]octan-2-one 124

A solution of 119 and 120 (1:1, 46.2 mg, 0.188 mmol) and W2-Raney nickel (excess) in benzene (3 mL) was stirred at room temperature for 6 h. The reaction mixture was filtered through a pad of Celite and the catalyst was washed with hot benzene. The combined organic solvents were removed in vacuo to afford 123 and 124 (19.6 mg, 76%)

as a light yellow oil. ^{1}H nmr analysis indicates that 123 and 124 are present in a 1:1 ratio. tlc: R_f 0.25, 0.30 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1704 cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$) δ : 2.64, 2.49 (m, 1H), 2.27, 2.13 (m, 1H), 1.50-2.07 (m, 6H), 1.26 (m, 1H), 1.18, 1.13 (d, 3H, J=7.5 Hz, $\underline{CH_3}CH$), 0.90-1.13 (m, 2H), 0.51, 0.37 (m, 1H); hreims: m/z calcd. for $C_9H_{14}O_1$ (M^+): 138.1045; found: 138.1050 (23), 120 (13), 94 (84), 83 (44), 82 (42), 81 (70), 79 (31), 67 (78), 55 (100); cims: m/z 277 ($2M^+$+1,55), 156 (M^++18, 85), 138 (M^+, 100).

(2RS,6SR)-2,6-Dimethylcycloheptanone 125 and (2SR,6SR)-2,6-Dimethylcycloheptanone 126

A solution of 119 and 120 (1:1 mixture, 161.1 mg, 0.654 mmol) and freshly prepared W2-Raney nickel (excess) in benzene (4 mL) was stirred at room temperature for 12 h. The reaction mixture was filtered through a pad of Celite and the catalyst was washed with hot benzene. The combined organic solvents were removed in vacuo. Bulb to bulb distillation of the residue afforded 125 and 126 (61.2 mg, 67%) as a colorless liquid. ^{1}H and ^{13}C nmr analysis indicate that 125 and 126 are present in a 1:1 ratio. b.p.: 125°C/721 torr; tlc: R_f 0.31 (1:9 ethyl acetate/Skellysolve B); ftir (neat): 1702 cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$) δ: 2.53 (m, 1H, $\underline{CH}CH_3$), 2.44 (m, 2H,

$CH_2C{=}O$), 1.87 (m, 2H), 1.87 (m, 1H, $\underline{CH}CH_3$) 1.63 (m, 1H), 1.36 (m, 2H), 1.17 (m, 1H), 1.07, 1.05 (d, 3H, J=7 Hz, $\underline{CH_3}CH$), 1.00, 0.98 (d, 3H, J=6 Hz, $\underline{CH_3}CH$); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 215.9 + 215.1 (s), 50.2 + 49.8 (t), 47.3 + 46.4 (s), 38.9 + 38.4 (t), 33.6 + 31.8 (t), 31.7 + 31.6 (d), 28.0 + 28.0 (t), 23.9 + 22.5 (q), 18.0 + 16.4 (q); hreims: m/z calcd. for $C_9H_{16}O$ (M^+): 140.1201; found: 140.1201 (53), 125 (10), 112 (67), 82 (43), 69 (100), 56 (42), 55 (50).

Dimethylene bisthiochloroformate 133

(Reaction must be conducted in fume hood.)

A 500-mL three necked round bottom flask equipped with a dry ice condenser under a nitrogen atmosphere was cooled to -78°C (dry ice-acetone bath) and phosgene (144 mL, 2.03 mol) was condensed into the flask. Dry pyridine (1 mL, 0.012 mol) was added by means of a syringe and the reaction mixture was allowed to warm to 0°C in an ice-water bath. Ethanedithiol (42 mL, 0.481 mol) was added by means of a pressure equalized dropping funnel over a 2 h period. The ice-water bath was removed and the reaction mixture was stirred for 12 h. Excess phosgene was removed in vacuo and Et_2O (200 mL) was added. The reaction mixture was filtered through Celite and the solvent removed in vacuo to afford 133 (103.2 g, 98%) as a yellow

solid. m.p.: 40-41°C; tlc: R_f 0.35 (1:10 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1761, 1670 cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$) δ: 3.25 (s); hreims: m/z calcd. for $C_4H_4O_2S_2Cl$ (M^+-Cl, parent ion not seen): 182.9342; found: 182.9339 (13), 124 (35), 123 (100).

Gas phase decomposition of dimethylene bisthiochloroformate 133

The pyrolysis apparatus was similar to that used for the pyrolysis of ethylene glycol bischloroformate described elsewhere.[74] The vertical pyrolysis tube was made of Pyrex (300 x 10 mm or 330 x 25 mm) and placed in the centre of a cylindrical heater. The pressure equalized dropping funnel (25 mL) was equipped with a helium inlet and a Teflon adjustable stopcock. It was connected to the top portion of the vertical tube. The bottom of the vertical tube was connected to a 100 mL round bottom flask cooled to -78°C in a dry ice-acetone bath. The side arm outlet of the flask was vented to the atmosphere. Prior to the addition of 133 the system was flushed with helium through the top of the funnel. Compound 133 (m.p.: 40-41°C) was heated gently until it became a liquid, then it was dropped at the rate of 1-2 g per min onto the packed column. During the pyrolysis the helium stream was maintained at a fixed flow rate (either

60 or 6 mL per min). After the pyrolysis was completed the pyrolysate mixture was weighed and analyzed by ^1H nmr spectroscopy. When the pyrolysis was conducted up to and including 450°C only decomposition of 133 was observed along with the formation of 134. At 511°C in addition to the formation of 134 (17%) a small amount of the desired 129 was formed (3%) as shown by ^1H nmr signals at δ 6.75 (dd, 1H, J=10, 17 Hz), δ 5.57 (d, 1H, J=17 Hz), and δ 5.54 (d, 1H, J=10 Hz). However, extensive decomposition of 133 was observed and the formation of 129 was not reproducible.

One compound that was consistently produced in all decomposition studies was 134 which displays the following properties: m.p.: 39-40°C; tlc: R_f 0.15 (1:9 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1715, 1670, 1634 cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$) δ: 3.74 (s); hreims: m/z calcd. for $C_3H_4S_2O$ (M^+): 119.9704; found: 119.9707 (100), 92 (75), 64 (41), 60 (39), 58 (83).

3-Thia-dodec-1-en-4-one 137

Vinyl lithium (4.65 mL, 9.8 mmol, 2.1 M solution in THF) was cooled to -78°C in a dry ice-acetone bath and styrene sulfide[76c] (1.8 mL, 14.6 mmol) was added by means of a syringe. The resulting solution was stirred at -78°C for 2.5 h. Nonanoyl chloride (2.63 mL, 14.6 mmol) was

added and the resulting solution was stirred for 0.5 h at -78°C and then allowed to warm to 25°C. Water (5 mL) was added and the reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organic extracts were washed with satd NaCl, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the residue by flash chromatography eluting with 1:99 ethyl acetate/Skellysolve B afforded **137** (785.3 mg, 40%) as a colorless oil. tlc: R_f 0.46 (1:19 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1710 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 6.90 (dd, 1H, J=10, 17 Hz, CH_2=CHS), 5.50 (d, 1H, J=10 Hz, CH_2=CHS), 5.47 (d, 1H, J=17 Hz, CH_2=CHS), 2.57 (t, 2H, J=7.5 Hz, CH_2C=O), 1.67 (m, 2H), 1.27 (m, 10H), 0.87 (t, 3H, J=6.5 Hz, CH_3); hreims: m/z calcd. for $C_{11}H_{20}OS$ (M^+): 200.1235; found: 200.1239 (9), 141 (100), 71 (54).

3,5,5-Trimethyl-2-[(4-chloro-2-thiabutanoyl)oxy]cyclohex-2-enone **143**

A solution of alcohol **31** (80.3 mg, 0.52 mmol), pyridine (15 drops), S-(β-chloroethyl)chlorothiolformate **144** (15 drops, prepared according to reported procedure[82,83]) and CH_2Cl_2 (5 mL) was stirred at room temperature for 6 h and then washed with 5% HCl (10 mL) and satd $NaHCO_3$ (10 mL). The aqueous layers were washed with CH_2Cl_2 (2 x 10 mL) and the combined organic extracts were dried

(Na_2SO_4), filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography eluting with 1:10 ethyl acetate/Skellysolve B afforded 143 (118.6 mg, 83%) as a white solid. A portion of 143 was recrystallized from diethyl ether/Skellysolve B to afford 143 as colorless crystals. m.p.: 77-78°C; tlc: R_f 0.16 (1:10 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1726, 1688, 1655 cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$) δ : 3.74 (t, 2H, J=7 Hz, $\underline{CH_2}CH_2$), 3.23 (t, 2H, J=7 Hz, $\underline{CH_2}CH_2$), 2.38 (s, 4H, 2 x CH_2) 1.88 (s, 3H, $CH_3C{=}C$), 1.08 (s, 6H, 2 x CH_3); ^{13}C nmr (50.3 MHz, $CDCl_3$)δ : 190.1 (s), 168.2 (s), 145.8 (s), 141.7 (s), 50.8 (t), 45.1 (t), 42.2 (t), 33.2 (s), 33.1 (t), 27.9 (2q), 17.8 (q); hreims: m/z calcd. for $C_{12}H_{17}O_3SCl$ (M^+): 276.0586; found: 276.0581 (1), 181.12 (65), 181.09 (100), 180 (37), 154 (30), 137 (32), 83 (30), 69 (39), 63 (80). Analysis: calcd. for $C_{12}H_{17}O_3SCl$: C 52.07, H 6.19, O 17.34, Cl 12.81; found: C 51.84, H 6.12, O 17.62, Cl 12.97.

3,5,5-Trimethyl-2-[(4-iodo-2-thiabutanoyl)oxy]cyclohex-2-enone 145

A mixture of 143 (45.0 mg, 0.163 mmol) and NaI (314.2 mg, 2.096 mmol) in methyl ethyl ketone (3 mL) was heated under reflux for 18 h. The solvent was removed in vacuo

and CH_2Cl_2 (5 mL) and H_2O (5 mL) was added. The aqueous layer was extracted with additional CH_2Cl_2 (2 x 10 mL), the combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give 145 (66.5 mg, 111%) as a red oil. tlc: R_f 0.35 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1725, 1688, 1657 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 3.36 (m, 4H, CH_2CH_2) 2.37 (s, 4H, 2 x CH_2), 1.88 (s, 3H, $CH_3C{=}C$), 1.09 (s, 6H, 2 x CH_3); ^{13}C nmr (50.3 MHz, $CDCl_3$) δ: 190.0 (s), 167.9 (s), 145.7 (s), 141.6 (s), 50.7 (t), 45.0 (t), 33.6 (2t), 33.0 (s), 27.9 (2q), 17.8 (q); hreims: m/z calcd. for $C_{11}H_{17}O_2$ (M^+-COSI, parent ion not seen): 181.1228; found: 181.1199 (100), 154 (37), 83 (44); cims: m/z 386 (M^++18, 100).

3,3-Dimethyl-5-methylene-7,9-dioxabicyclo[4.3.0]non-1-en-8-one 146

A solution of compound 145 (5.0 mg, 0.014 mmol) and dry Et_3N (1 drop) in dry DMSO (0.5 mL) was heated at 75°C in an oil bath for 12 h, then H_2O (1 mL) was added. The reaction mixture was extracted with Et_2O (2 x 5 mL). The organic extracts were combined, washed with satd NaCl, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give after ptlc (1:19 ethyl acetate/Skellysolve B) 146 (2.1 mg, 86%) as a colorless oil. tlc: R_f 0.28 (1:10 ethyl

acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1820, 1630 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.17 (brs, 1H, C=CH_2), 4.95 (brs, 1H, C=CH_2), 2.37 (s, 2H, CH_2), 2.22 (brt, 2H, J=1.5 Hz, CH_2), 1.07 (s, 6H, 2 x CH_3); hreims: m/z calcd. for $C_{10}H_{12}O_3$ (M^+): 180.0787; found: 180.0785 (32), 113 (38), 87 (100), 57 (36); cims: m/z 198 (M^++18, 100).

Bis-2-(3,5,5-trimethylcyclohex-2-enoyl)carbonate 147

A solution of compound 145 (13.6 mg, 0.049 mmol) and dry DBU (5 drops) in dry ArH (3 mL) was stirred at room temperature for 12 h. Et_2O (5 mL) was added and the reaction mixture was washed with 5% HCl and satd $NaHCO_3$. The aqueous layer was extracted with additional Et_2O (2 x 5 mL), the organic layers combined, washed with satd NaCl, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Ptlc of the residue with 1:4 ethyl acetate/Skellysolve B afforded the following three products: 146 (2.2 mg, 25%, *vide supra*), 31 (3.1 mg, 41%), and 147 (1.6 mg, 10%). Compound 147 displays the following properties: m.p.: 150-151°C; tlc: R_f 0.14 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1765, 1687, 1661 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 2.37 (s, 4H, 2 x CH_2), 2.01 (s, 3H, CH_3C=C), 1.09 (s, 6H, 2 x CH_3); hreims: m/z calcd. for $C_{10}H_{13}O_3$ (M^+ - $C_9H_{13}O_2$, parent ion not seen): 181.0865;

found: 181.0860 (100), 180 (46), 137 (63), 81 (89), 67 (30); cims: m/z 352 (M^++18, 100).

3,5,5-Trimethyl-2-[(4-phenylseleno-2-thiabutanoyl)oxy]-cyclohex-2-enone 148

Diphenyl diselenide (634.4 mg, 2.03 mmol) and sodium hydride (185.0 mg, 3.85 mmol, 50% dispersion in mineral oil) were placed in an oven-dried, 25 mL, one necked round bottom flask equipped with a rubber septum cap and a condensor. The flask and its contents were evacuated (oil pump) and flushed with nitrogen three times. Dry THF (8 mL) was added to the contents of the flask using a syringe and the mixture was heated under reflux for 1 h yielding a light yellow suspension of the sodium phenylselenide. The reaction mixture was allowed to cool to room temperature and dry, oxygen-free HMPA (0.4 mL) was added using a syringe. The resulting homogeneous orange solution was cooled to -78°C in a dry ice-acetone bath and a solution of compound 145 (1.308 g, 3.55 mmol) in dry THF (2 mL) was added. The reaction mixture was stirred at -78°C for 30 min and was quenched by the addition of satd NH_4Cl (3 mL). Water (10 mL) was added and the reaction mixture was extracted with CH_2Cl_2 (3 x 30 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification of the residue by flash column chromatography eluting with 12:88 ethyl acetate/

Skellysolve B afforded 148 (1.379 g, 98%) as a dark yellow oil. tlc: R_f 0.05 (1:19 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1723, 1688, 1655, 1580 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 7.49 (m, 2H, ArSe), 7.23 (m, 3H, ArSe), 3.16 (s, 4H, SCH_2CH_2Se), 2.37 (s, 4H, 2 x CH_2), 1.86 (s, 3H, $CH_3C{=}C$), 1.10 (s, 6H, 2 x CH_3), ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 190.2 (s), 168.7 (s), 145.3 (s), 142.0 (s), 133.1 (2d), 129.2 (2d), 129.0 (s), 127.3 (d) 51.1 (t), 45.5 (t), 33.2 (s), 31.9 (t), 28.1 (q), 26.5 (t), 18.0 (q); hreims: m/z calcd. for $C_{18}H_{22}O_3SSe$ (M^+): 398.0454; found: 398.0460 (26), 217 (48), 185 (100), 183 (63), 181 (31), 157 (54), 77 (37).

3,5,5-Trimethyl-2-[(2-thiabut-3-enoyl)oxy]cyclohex-2-enone 127

A solution of selenide 148 (1.379 g, 3.47 mmol) and pyridine (0.6 mL, 7.42 mmol) in dry CH_2Cl_2 (30 mL) was cooled to 0°C in an ice-water bath and hydrogen peroxide (1.8 ml, 17.6 mmol, 30% solution in H_2O) was added. The reaction mixture was stirred at 0°C for 30 min and then satd $NaHCO_3$ was added. The aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL). The organic extracts were combined, washed with 5% HCl, dried (Na_2SO_4) filtered, and concentrated in vacuo. Purification of the residue by flash column chromatography eluting with 1:9 ethyl

acetate/Skellysolve B afforded 127 (515.4 mg, 62%) as a colorless oil. An analytical sample of 127 was prepared by bulb to bulb distillation. b.p.: 120°C/0.6 torr; tlc: R_f 0.12 (1:9 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1728, 1683, 1657, 1595 cm^{-1}; uv (methanol) λ^emax: 231 (ε 16252) nm: ^1H nmr (400 MHz, $CDCl_3$) δ : 6.72 (dd, 1H, J=10, 17 Hz, $\underline{CH}$=CH_2), 5.531 (d, 1H, J=10 Hz, CH=$\underline{CH_2}$), 5.528 (d, 1H, J=17 Hz, CH=$\underline{CH_2}$), 2.38 (s, 4H, 2 x CH_2), 1.88 (s, 3H, CH_3C=C), 1.10 (s, 6H, 2 x CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 190.3 (s), 166.7 (s), 146.0 (s), 141.7 (s), 126.0 (d), 118.2 (t), 50.9 (t), 45.2 (t), 33.2 (s), 28.0 (2q), 17.9 (q); hreims: m/z calcd. for $C_{10}H_{13}O_3$ (M^+-C_2H_3S, parent ion not seen): 181.0864; found: 181.0866 (100), 137 (42), 81 (69); Analysis: calcd. for $C_{12}H_{16}O_3S$: C 59.97, H 6.71, S 13.34; found: C 59.88, H 6.54, S 13.60.

(1RS,6RS,8RS)-Carbonyloxythia-4,4,6-trimethylbicyclo-[4.2.0]octan-2-one 128

A degassed solution of 127 (515.4 mg, 2.15 mmol) in dry acetone (100 mL) was irradiated using a 200-W medium pressure mercury lamp in a Pyrex immersion well through a Pyrex filter (total thickness of Pyrex ca. 4.5 mm) for 15.5 h. The solvent was removed in vacuo. The residue was purified by flash chromatography eluting with

1:3 ethyl acetate/Skellysolve B to afford unreacted 127 (54.2 mg, 11%), and 128 (389.6 mg, 76%).

In a separate experiment a degassed solution of 127 (104.0 mg, 0.433 mmol) in dry acetone (200 mL) was irradiated through a Uranium filter using a 450-W medium pressure mercury lamp for 22.5 h. The solvent was removed in vacuo. The residue was purified by flash chromatography eluting with 1:3 ethyl acetate/Skellysolve B to afford unreacted 127 (16.7 mg, 16%) and 128 (63.5 mg, 61%, m.p. 142-143°C).

An analytical sample of 128 was prepared by recrystallization from dichloromethane/Skellysolve B. Compound 128 displays the following properties: m.p.: 146-147°C; tlc: R_f 0.13 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1732, 1705 cm^{-1}; uv (methanol) λ max: 205 (ε 2043) nm; ^1H nmr (200 MHz, $CDCl_3$) δ : 4.37 (t, 1H, J=7.5 Hz, $CH_2\underline{CH}S$), 2.59 (d, 1H, J=15 Hz, $CH_2C{=}O$), 2.58 (dd, 1H, J=7.5, 12.5 Hz, $\underline{CH_2}CHS$), 2.39 (dd, 1H, J=2.5, 15 Hz, $CH_2C{=}O$), 2.22 (dd, 1H, J=7.5, 12.5 Hz, $\underline{CH_2}CHS$), 2.00 (d, 1H, J=14.5 Hz, CH_2), 1.89 (dd, 1H, J=2.5, 14.5 Hz, CH_2), 1.35 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.00 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ : 202.0 (s), 173.5 (s), 90.2 (s), 51.7 (t), 50.5 (t), 47.1 (t), 45.0 (s), 43.6 (d), 34.8 (s), 31.4 (q), 26.8 (q), 24.6 (q); hreims: m/z calcd. for $C_{12}H_{16}O_3S$ (M^+):

240.0820; found: 240.0824 (26), 225 (10), 96 (100), 83 (36); Analysis: calcd. for $C_{12}H_{16}O_3S$: C 59.97, H 6.71, S 13.34; found: C 60.09, H 6.68, S 13.30.

(1RS,6RS)-1-Hydroxy-4,4,6-trimethylbicyclo[4.2.0]octan-2-one 150 and (1RS,5SR)-1-Hydroxy-5,7,7-trimethylbicyclo-[3.3.0]octan-2-one 151

A mixture of 128 (123.2 mg, 0.513 mmol) and excess W2-Raney nickel in EtOH (4 mL) was stirred at room temperature for 12 h. The reaction mixture was filtered through a pad of Celite and the nickel was washed with hot MeOH. The solvent was removed in vacuo and the residue was purified by flash chromatography eluting with 1:9 ethyl acetate/Skellysolve B to afford 150 (25.2 mg, 27%), 151 (27.9 mg, 30%) and unreacted 128 (11.6 mg, 9%). Compound 150 (colorless crystals) displays the following properties: m.p.: 59-60°C; tlc: R_f 0.27 (1:3 ethyl acetate/ Skellysolve B); ftir ($CHCl_3$, cast): 3415, 1736 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$)δ : 2.58 (brs, 1H, OH), 2.52 (ddd, 1H, J=3.5, 10, 16 Hz, $\underline{CH_2}CH_2$), 2.25 (m, 1H, $\underline{CH_2}CH_2$), 1.95 (d, 1H, J=14 Hz, CH_2), 1.79 (m, 2H, $\underline{CH_2}CH_2$), 1.76 (s, 2H, CH_2), 1.55 (d, 1H, J=14 Hz, CH_2), 1.21 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.09 (s, 3H, CH_3); hreims: m/z calcd. for $C_{11}H_{18}O_2$ (M^+): 182.1307; found: 182.1307 (13), 126 (100), 111 (31); cims: m/z 200 (M^++18, 100).

Compound 151 (light yellow oil) displays the following properties: tlc: R_f 0.18 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3260, 1754 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 2.71 (brs, 1H, OH), 2.32 (m, 1H, $\underline{CH_2}CH_2$), 2.14 (m, 2H, $\underline{CH_2}CH_2$), 1.86 (m, 1H, $\underline{CH_2}CH_2$), 1.82 (d, 1H, J=13 Hz, CH_2), 1.76 (s, 2H, CH_2), 1.74 (d, 1H, J=13 Hz, CH_2), 1.36 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 0.94 (s, 3H, CH_3); hreims: m/z calcd. for $C_{11}H_{18}O_2$ (M^+): 182.1307; found: 182.1310 (14), 139 (100), 126 (49), 97 (37).

(1RS,2RS,6RS,8RS)-Carbonyloxythia-4,4,6-trimethylbicyclo-[4.2.0]octan-2-ol 152

A solution of 128 (19.2 mg, 0.080 mmol) in MeOH (3 mL) was cooled to 0°C in an ice-water bath and sodium borohydride (9.0 mg, 0.238 mmol) was added. The reaction mixture was stirred at 0°C for 0.5 h then satd NH_4Cl (5 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (3 x 15 mL). The organic layers were combined, dried (Na_2SO_4), filtered, and concentrated in vacuo to give 152 (19.85 mg, 96%) as a white solid: m.p.: 56-57°C; tlc: R_f 0.18 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3440, 1723 cm^{-1}; ^1H nmr (200 MHz, $CHCl_3$) δ: 4.11 (dd, 1H, J=5.5, 7.5 Hz, $CH_2\underline{CH}O$), 3.98 (dd, 1H, J=4, 6.5 Hz, $CH_2\underline{CH}S$), 2.41 (dd, 1H, J=7.5, 13 Hz,

$\underline{CH_2}CHO$), 2.16 (brs, 1H, OH), 2.06 (dd, 1H, J=5.5, 13 Hz, $\underline{CH_2}CHO$), 1.79 (dd, 1H, J=6.5, 14.5 Hz, $\underline{CH_2}CHS$), 1.67 (d, 1H, J=15, CH_2), 1.65 (dd, 1H, J=4, 14.5 Hz, $\underline{CH_2}CHS$), 1.49 (d, 1H, J=15 Hz, CH_2), 1.39 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); hreims: m/z calcd. for $C_{12}H_{18}SO_3$ (M^+): 242.0977; found: 242.0975 (5), 224 (14), 182 (25), 126 (34), 83 (31), 69 (32), 59 (45), 57 (100), 56 (34), 55 (63).

(1RS,2RS,6RS)-4,4,6-Trimethylbicyclo[4.2.0]octane-1,2-diol 153

A solution of 152 (15.3 mg, 0.063 mmol) and excess W2 Raney nickel in EtOH (3 mL) was stirred at room temperature for 12 h. The reaction mixture was filtered through a pad of Celite and the catalyst was washed with hot MeOH. The solvent was removed in vacuo and the residue was purified by flash chromatography eluting with 1:3 ethyl acetate/Skellysolve B to afford 153 (8.9 mg, 77%) as colorless needles. m.p.: 65-66°C; tlc: R_f 0.13 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3405 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 3.96 (dd, 1H, J=7, 8.5 Hz, $CH_2\underline{CH}O$), 2.27 (brs, 2H, 2 x OH), 2.03 (m, 2H), 1.67 (m, 1H), 1.41 (m, 3H), 1.22 (m, 2H), 1.19 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 0.96 (s, 3H, CH_3); hreims: calcd. for $C_{11}H_{20}O_2$(M^+): 184.1463; found: 184.1468 (36),

156 (94), 100 (100), 96 (32), 95 (44), 83 (50), 82 (40), 57 (41), 55 (42).

(1RS,6RS,8RS)-1,8-Carbonyloxythia-2,4,4,6-tetramethyl-bicyclo[4.2.0]oct-2-ene 154

A mixture of 128 (64.1 mg, 0.267 mmol) in dry THF (5 mL) was cooled to -78°C in a dry ice-acetone bath. Methyllithium (0.29 mL, 0.348 mmol, 1.2 M in diethyl ether) was added by means of a syringe and the resulting solution was stirred at -78°C for 1 h. Dry pyridine (0.043 mL, 0.534 mmol) and thionyl chloride (0.039 mL, 0.534 mmol) were then added separately by means of a syringe. The resulting solution was allowed to warm to room temperature and stirred for 1.5 h. Water (5 mL) and CH_2Cl_2 (10 mL) was added. The aqueous extracts were extracted with CH_2Cl_2 (2 x 20 mL). The organic extracts were combined, washed with 5% HCl, satd $NaHCO_3$, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residue was purified by flash chromatography using 1:9 ethyl acetate/Skellysolve B to afford 154 (56.2 mg, 88%) as colorless needles: m.p.: 75-76°C; tlc: R_f 0.36 (1:3 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 1729 cm^{-1}; ^1H nmr (200 MHz, $CDCl_3$) δ: 5.26 (d, 1H, J=1.5 Hz, C=CH), 3.98 (dd, 1H, J=5.5, 8 Hz, $CH_2\underline{CH}S$), 2.53 (dd, 1H, J=8, 13 Hz, $\underline{CH_2}CHS$), 2.00 (dd, 1H, J=5.5, 13 Hz, $\underline{CH_2}CHS$),

1.71 (d, 3H, J=1.5 Hz, CH_3C=C), 1.65 (d, 1H, J=14 Hz, CH_2), 1.48 (d, 1H, J=14 Hz, CH_2), 1.40 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.06 (s, 3H, CH_3); hreims: m/z calcd. for $C_{13}H_{18}SO_2$ (M^+): 238.1027; found: 238.1025 (4), 210 (14), 194 (48), 154 (43), 152 (100), 137 (92), 122 (30).

(1RS,6SR)-1-Hydroxy-2,4,4,6-tetramethylbicyclo[4.2.0]oct-2-ene 22

A solution of 154 (35.0 mg, 0.147 mmol) and excess W2 Raney nickel in EtOH (4 mL) was stirred at room temperature for 5 h. The reaction mixture was filtered through a pad of Celite and the catalyst was washed with hot MeOH. The solvent was removed in vacuo and the residue was purified by flash chromatography eluting with 1:9 ethyl acetate/Skellysolve B to afford 22 (20.4 mg, 77%) as colorless needles: m.p.: 59-60°C; tlc: R_f 0.17 (1:9 ethyl acetate/Skellysolve B); ftir ($CHCl_3$, cast): 3310, 1580 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$) δ: 5.32 (t, 1H, J=1.5 Hz, C=CH), 1.96 (m, 2H, $\underline{CH_2}CH_2$), 1.71 (d, 3H, J=1.5 Hz, CH_3C=C), 1.69 (m, 1H, $CH_2\underline{CH_2}$), 1.57 (brs, 1H, OH), 1.40 (d, 1H, J=14.5 Hz, CH_2), 1.30 (m, 1H, $CH_2\underline{CH_2}$), 1.22 (d, 1H, J=14.5 Hz, CH_2), 1.15 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 0.94 (s, 3H, CH_3); ^1H nmr (400 MHz, pyridine-d_5) δ: 5.36 (brs, 1H, $W_{\frac{1}{2}}$=3.5 Hz, C=CH), 3.60 (s, 1H, OH), 2.32 (m, 1H, $\underline{CH_2}CH_2$), 2.03 (m, 1H, $\underline{CH_2}CH_2$), 1.97 (d, 3H, J=1.5

Hz, $CH_3C{=}C$), 1.81 (m, 1H, $CH_2\underline{CH_2}$), 1.42 (d, 1H, J=14 Hz, CH_2), 1.37 (s, 3H, CH_3), 1.35 (m, 1H, $CH_2\underline{CH_2}$), 1.30 (d, 1H, J=14 Hz, CH_2), 1.11 (s, 3H, CH_3), 0.89 (s, 3H, CH_3); ^{13}C nmr (100.6 MHz, $CDCl_3$) δ: 135.8 (d), 132.7 (s), 73.0 (s), 45.0 (t), 43.2 (s), 33.4 (q), 31.8 (s), 31.3 (t), 30.7 (q), 25.0 (t), 24.2 (q), 17.1 (q); hreims: m/z calcd. for $C_{10}H_{16}O$ ($M^+-C_2H_4$, parent ion not seen): 152.1201; found: 152.1207 (46), 137 (100), 124 (50), 57 (60), 55 (48).

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